

Figure 1

BEST AVAILABLE COPY

Figure 2A

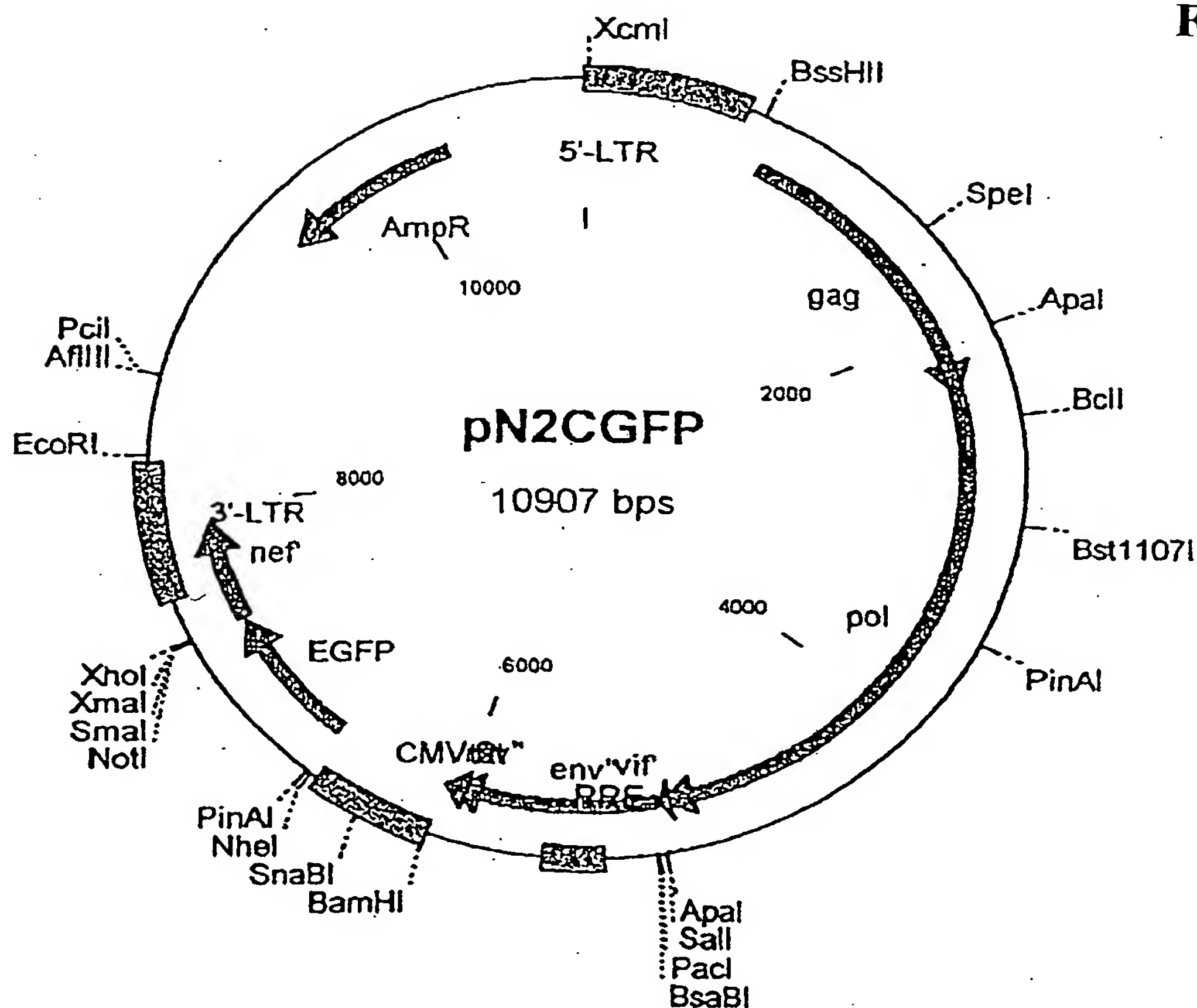
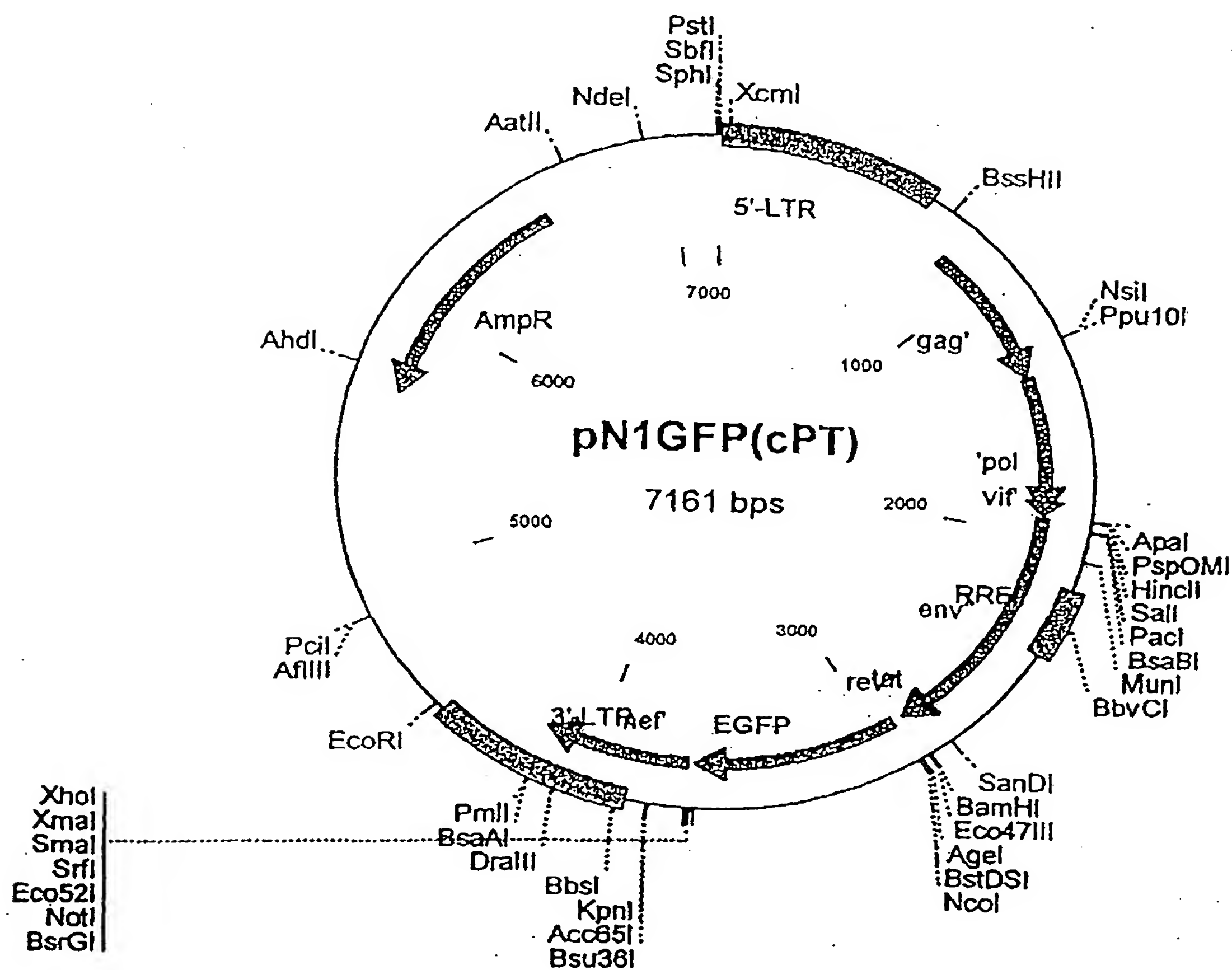


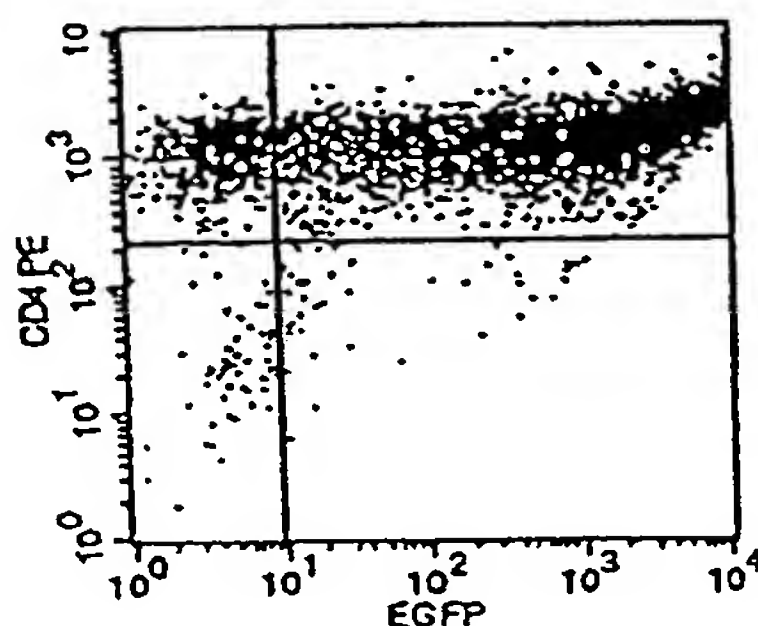
Figure 2B



BEST AVAILABLE COPY

Figure 3

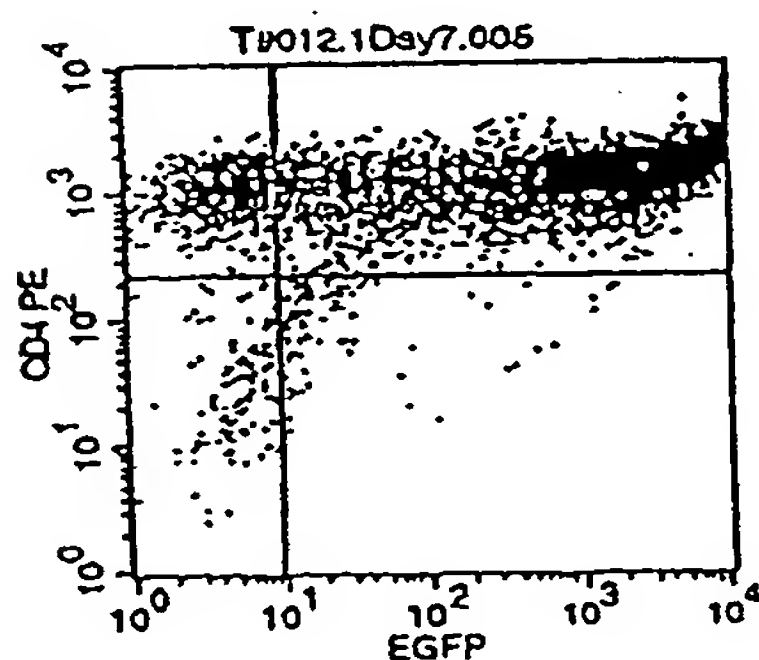
Panel
A



Stimulation Day 1

CD4+ EGFP+: 91.22%
 MF: 3325

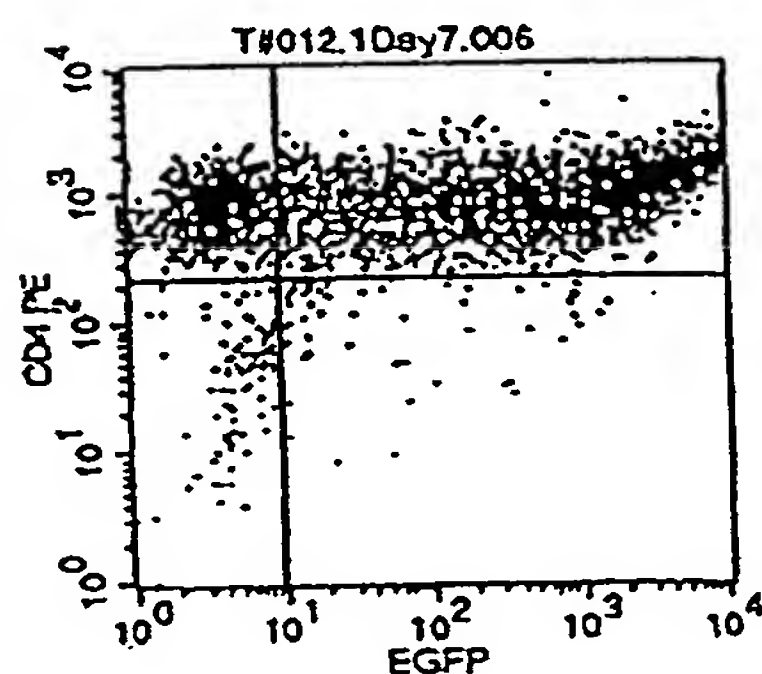
Panel
B



Stimulation Day 0
 Transduction Day 1

CD4+ EGFP+: 89.12%
 MF: 2962

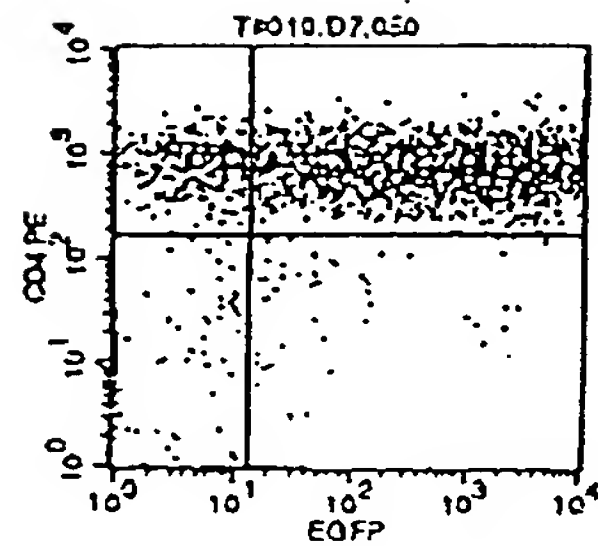
Panel
C



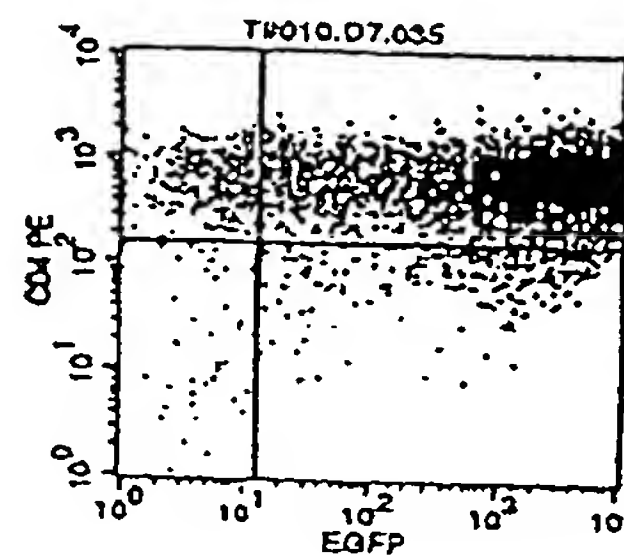
Stimulation Day 0
 Transduction Day 0

CD4+ EGFP+: 80.24%
 MF: 1966

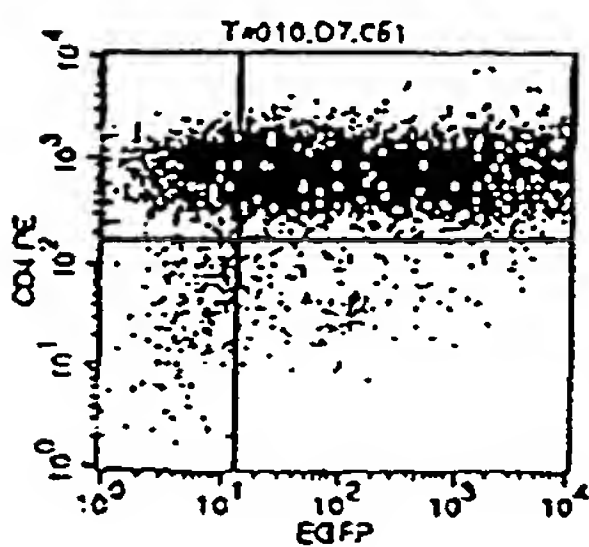
Figure 4



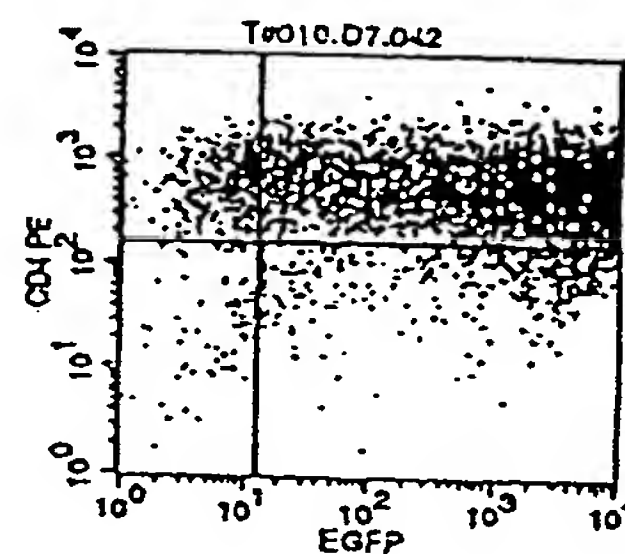
IL2/PHA-p
 CD4+ EGFP+: 84.5%
 MF: 1920



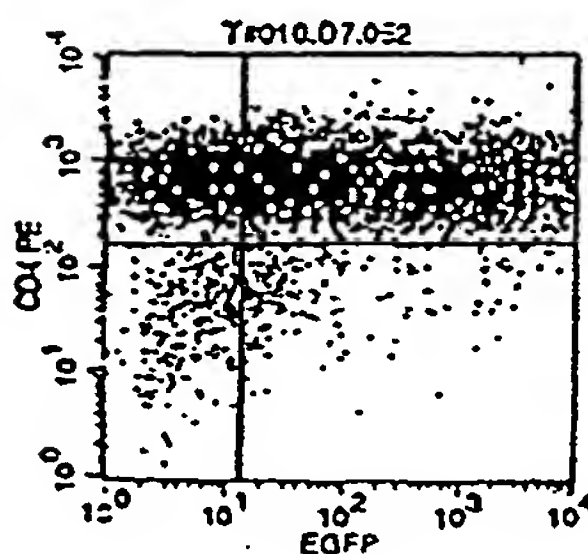
ICD3/ICD28
 CD4+ EGFP+: 96%
 MF: 5450



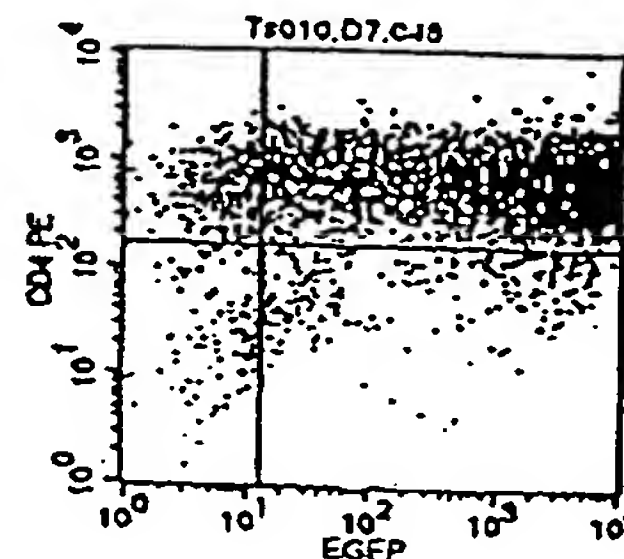
IL2/PHA-P
 CD4+ EGFP+: 80.95%
 MF: 1110



ICD3/ICD28
 CD4+ EGFP+: 95.5%
 MF: 5259



IL2/PHA-P
 CD4+ EGFP+: 70.2%
 MF: 863



ICD3/ICD28
 CD4+ EGFP+: 95.4%
 MF: 5346

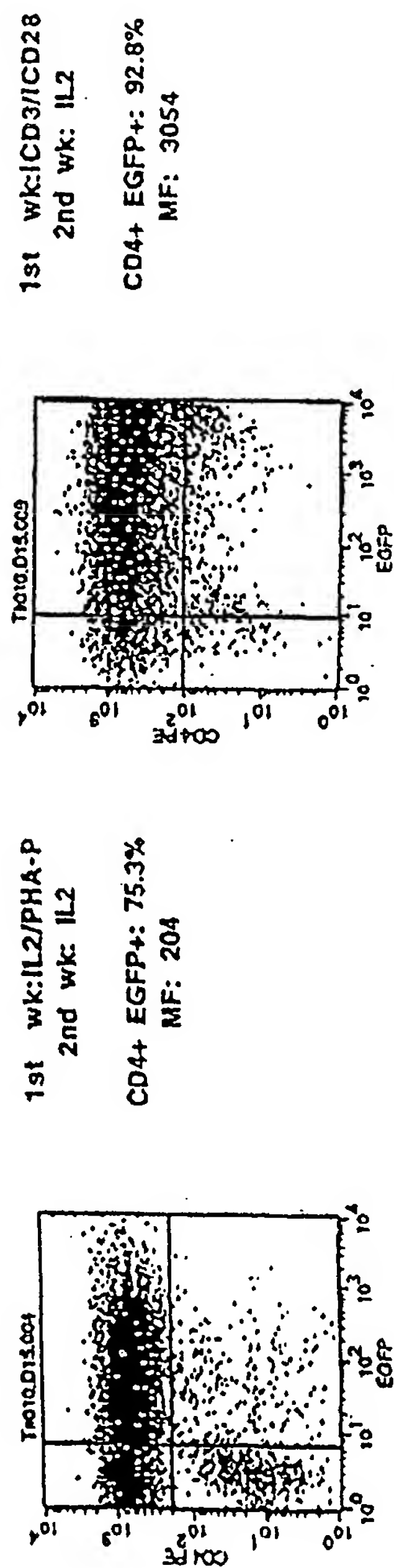
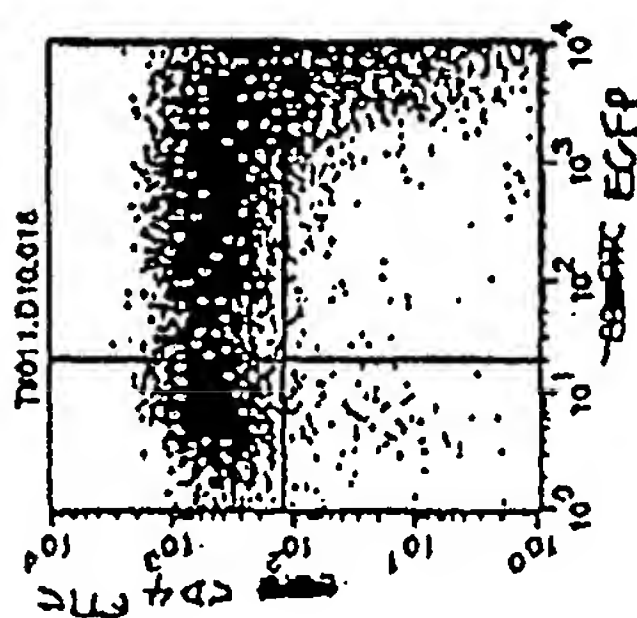


Figure 5

pN2CGFP @ MOI 20
 CD4+ EGFP+: 78.2%
 MF: 1966



pN1(cpt)CGFP @ MOI20
 CD4+ EGFP+: 77.1%
 MF: 1591

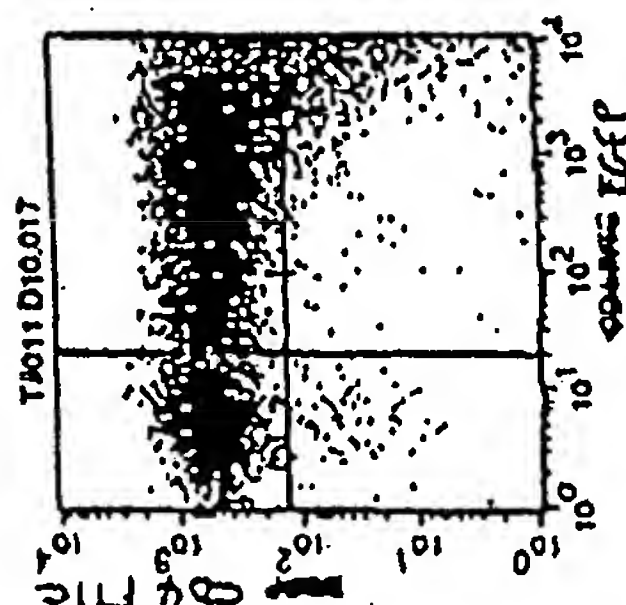
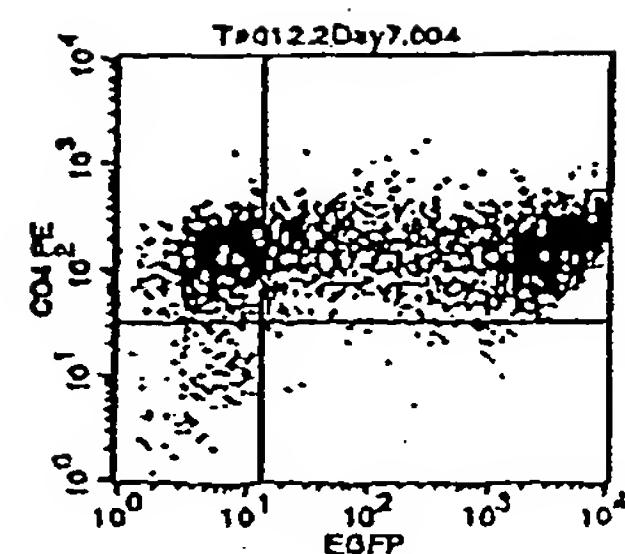
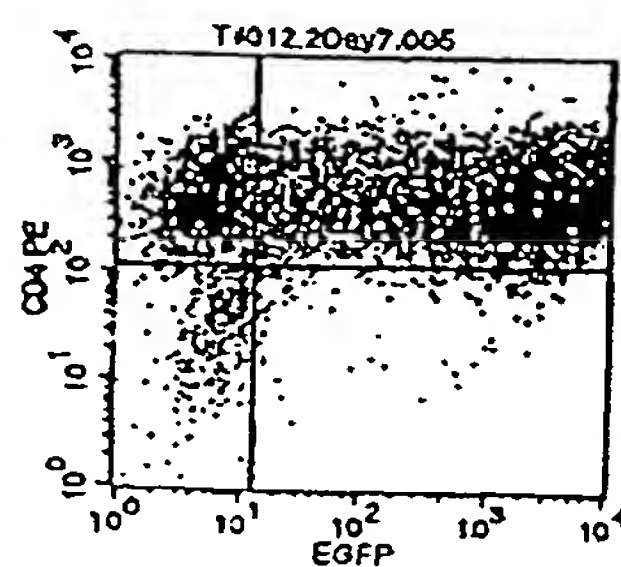


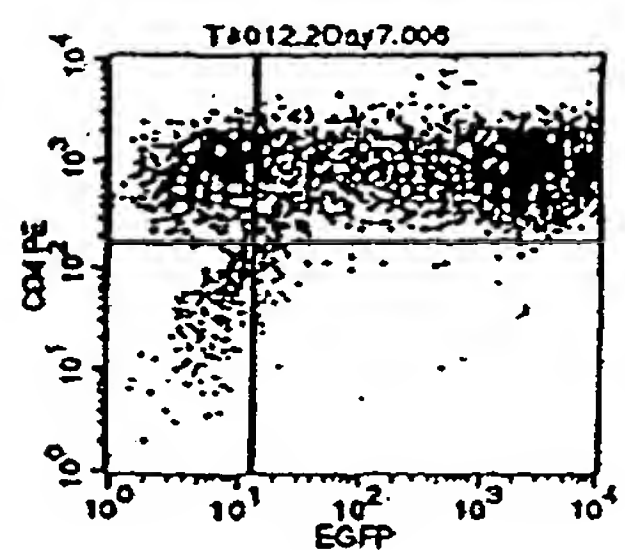
Figure 6



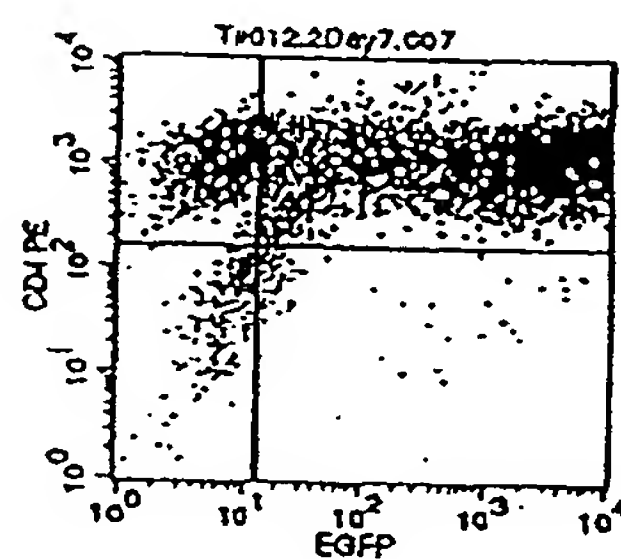
MOI 2
 CD4+ EGFP+: 72.7%
 MF: 3438



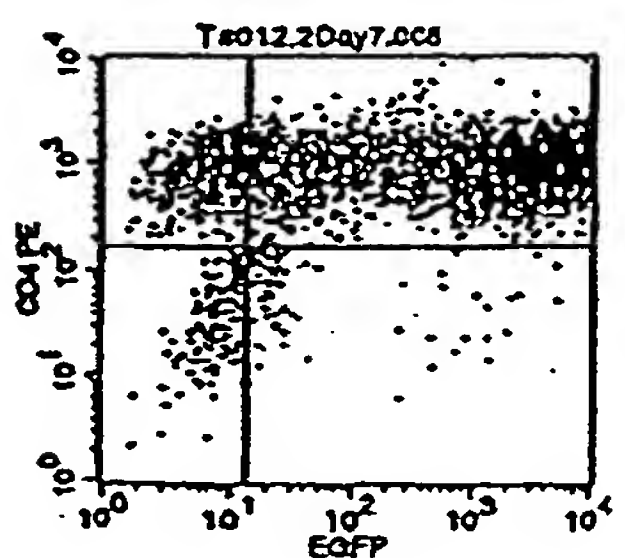
MOI 5
 CD4+ EGFP+: 75.4%
 MF: 2410



MOI 10
 CD4+ EGFP+: 79.7%
 MF: 2628



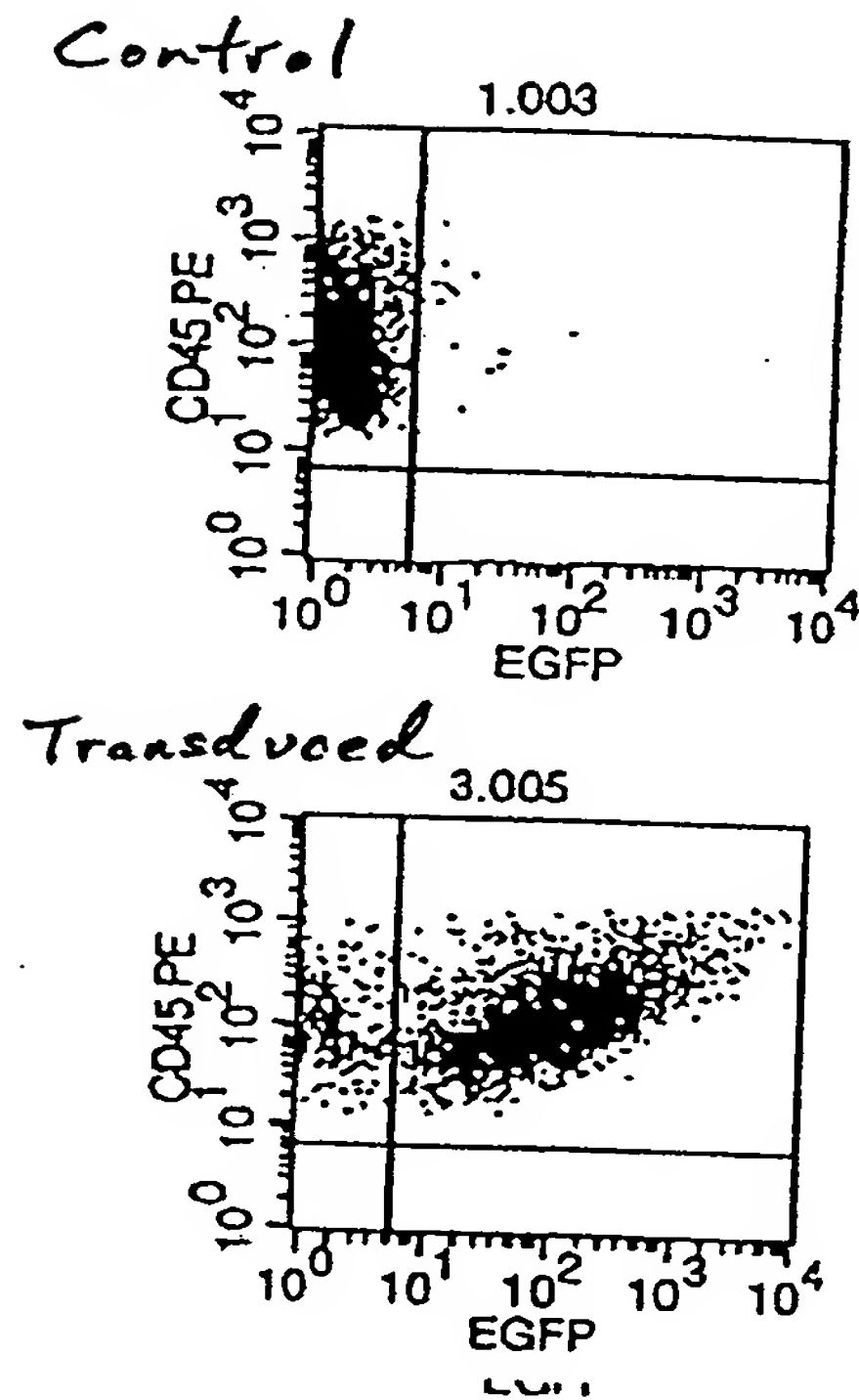
MOI 15
 CD4+ EGFP+: 82.4%
 MF: 2822



MOI 20
 CD4+ EGFP+: 83.8%
 MF: 2780

Figure 7

Figure 8



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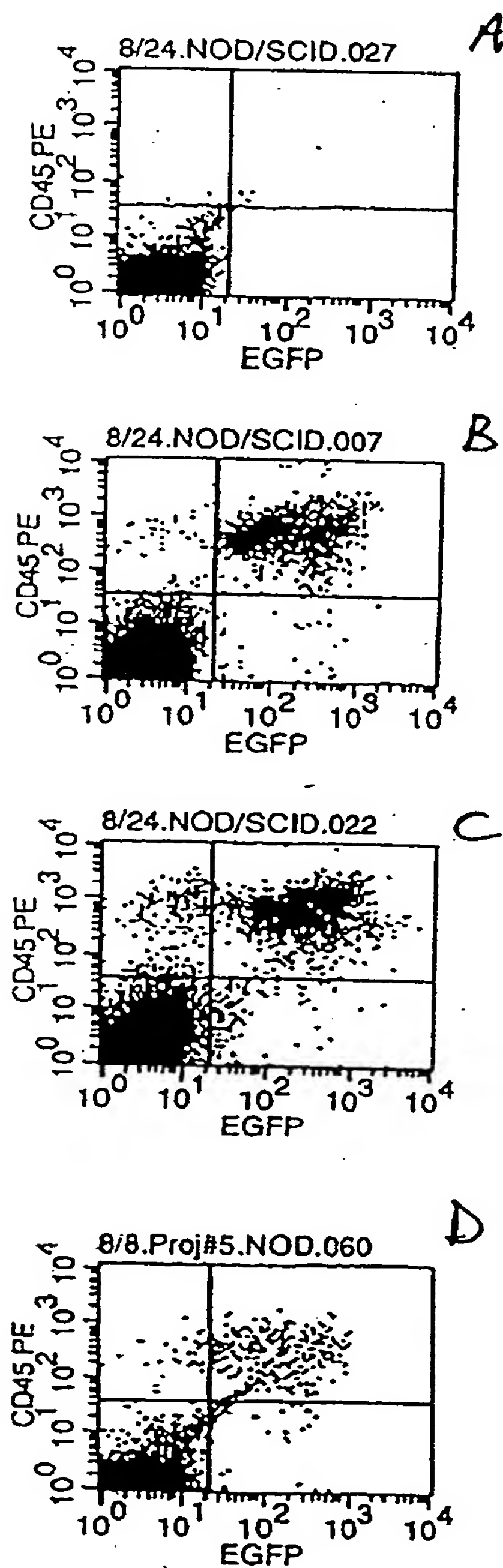


Figure 9

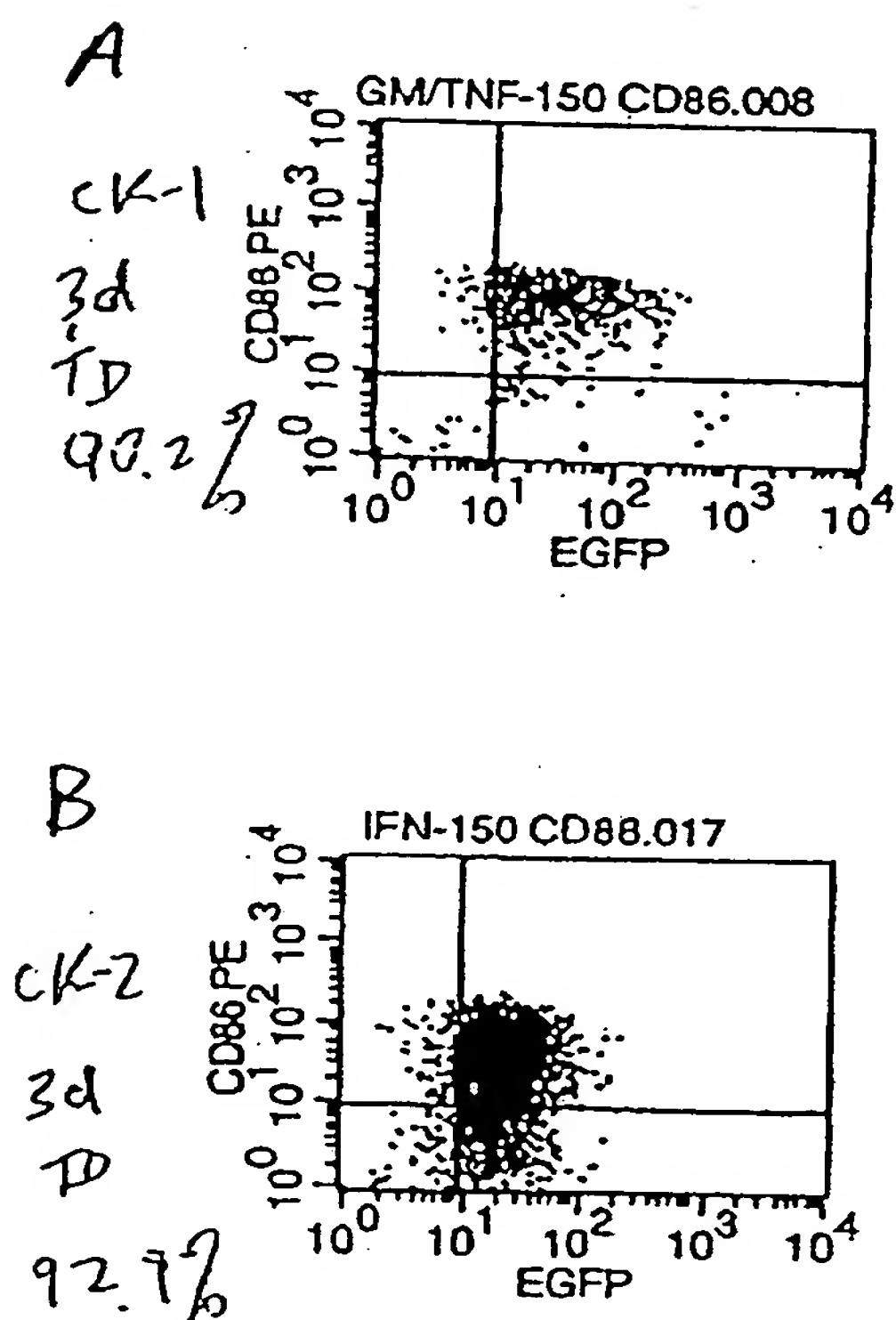


Figure 10

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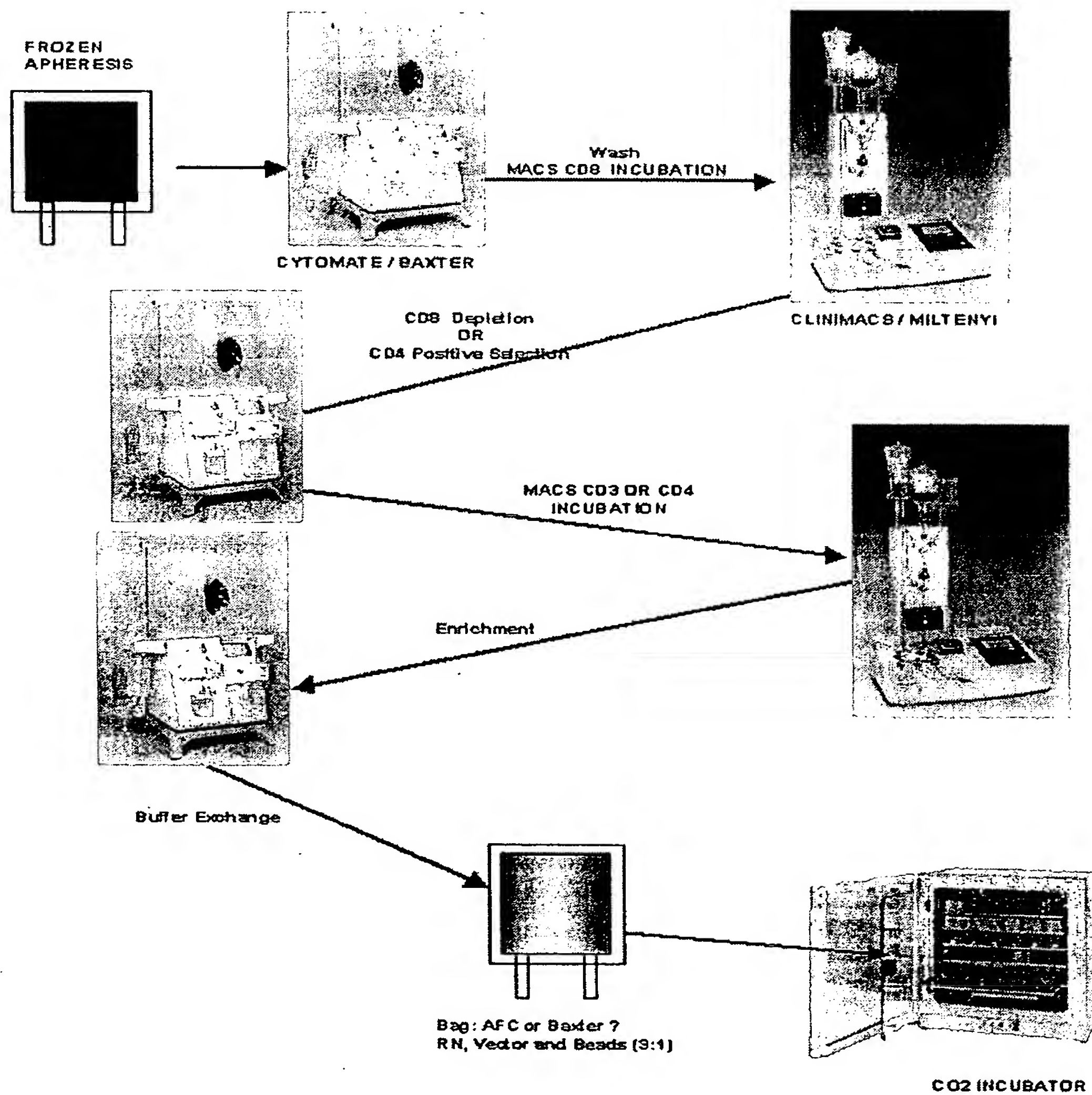


Figure 11

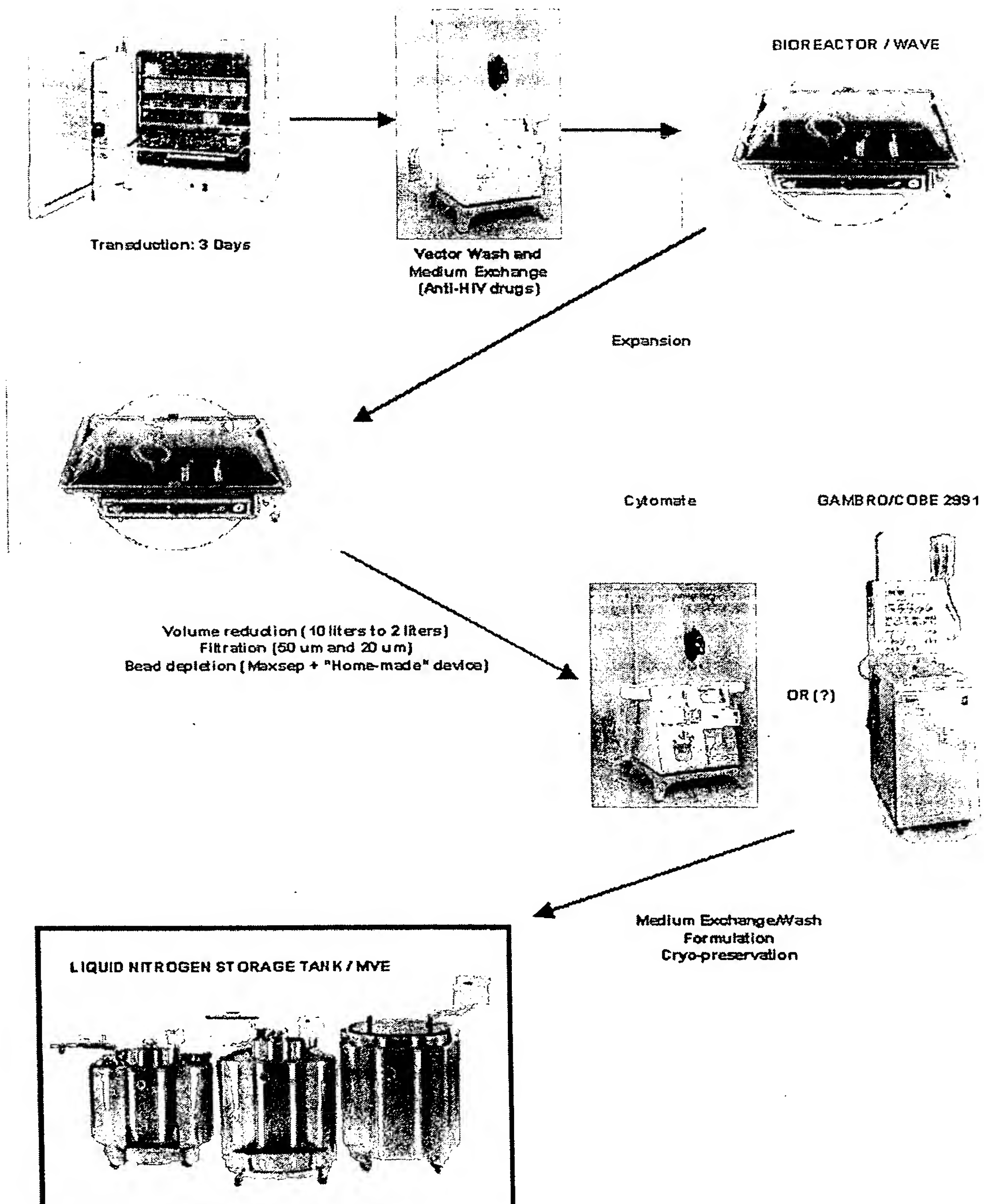


Figure 12

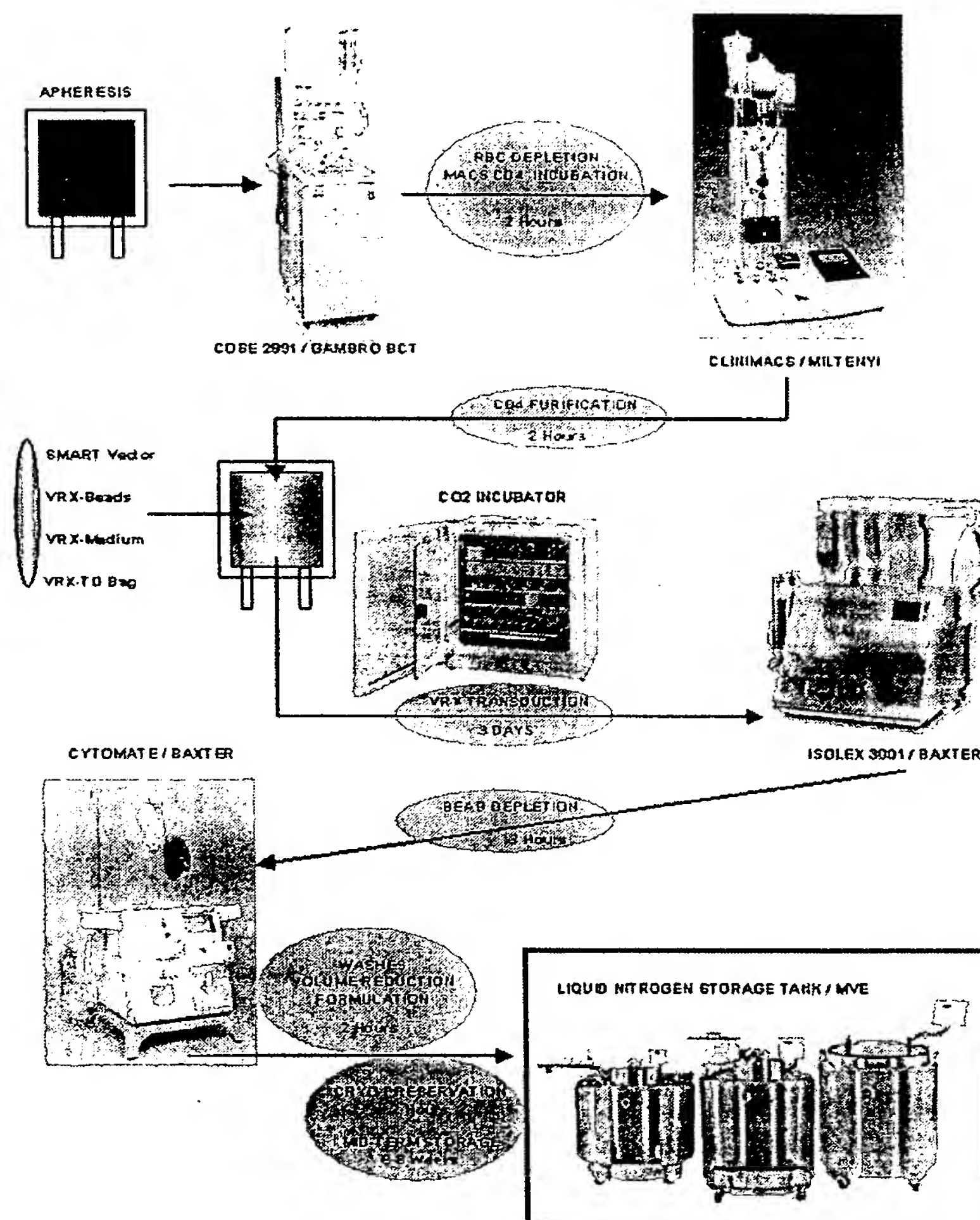


Figure 13

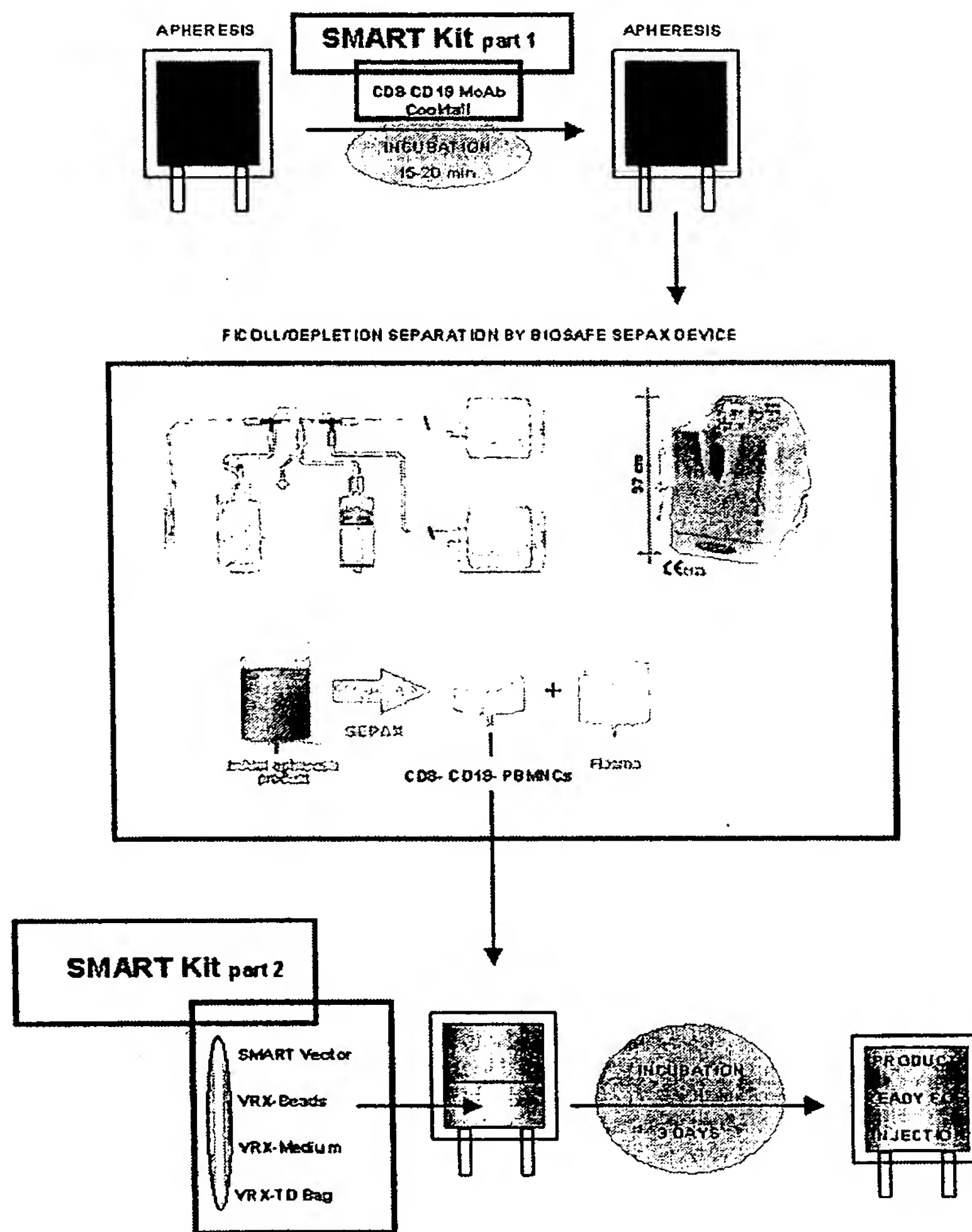


Figure 14

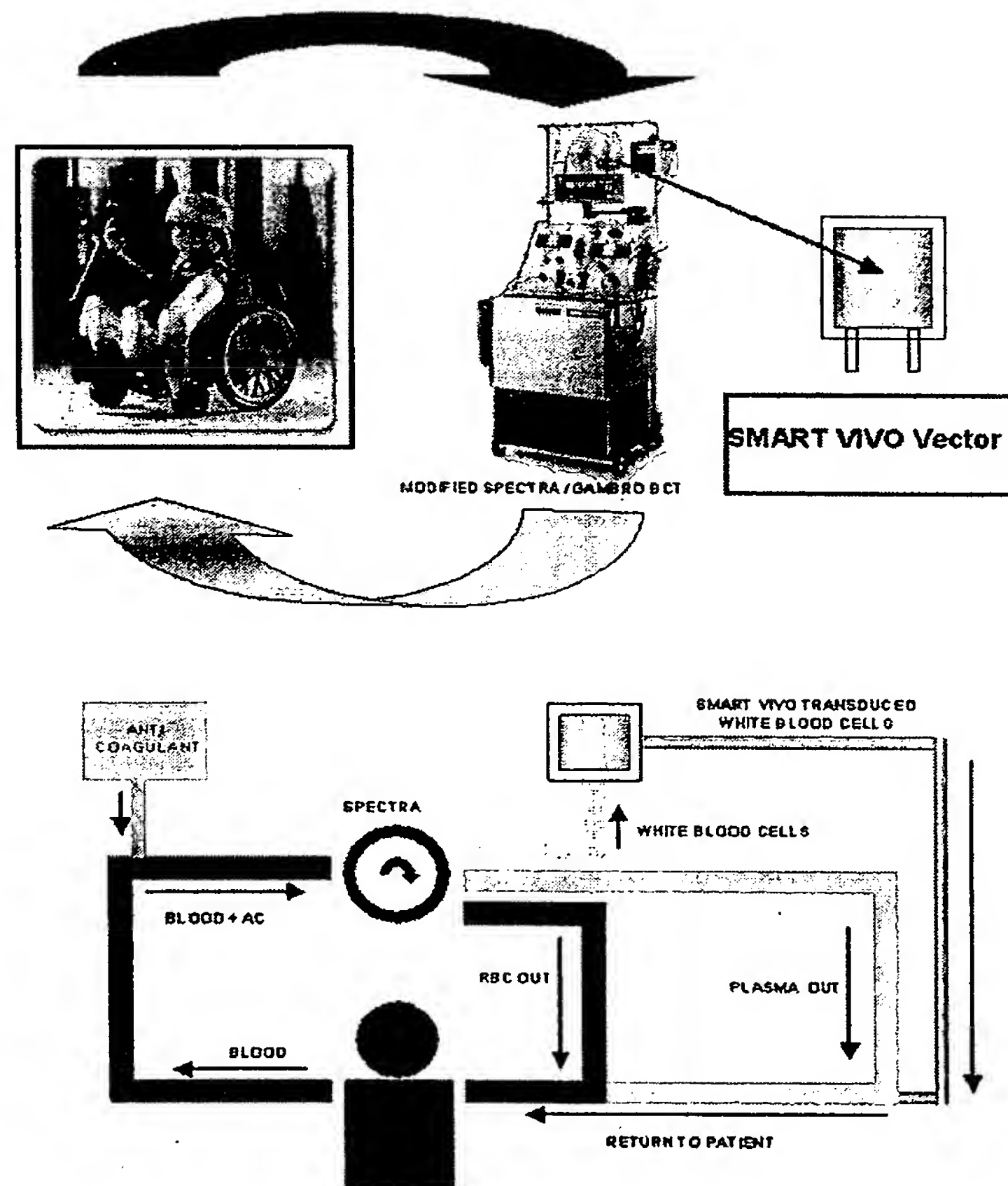


Figure 15

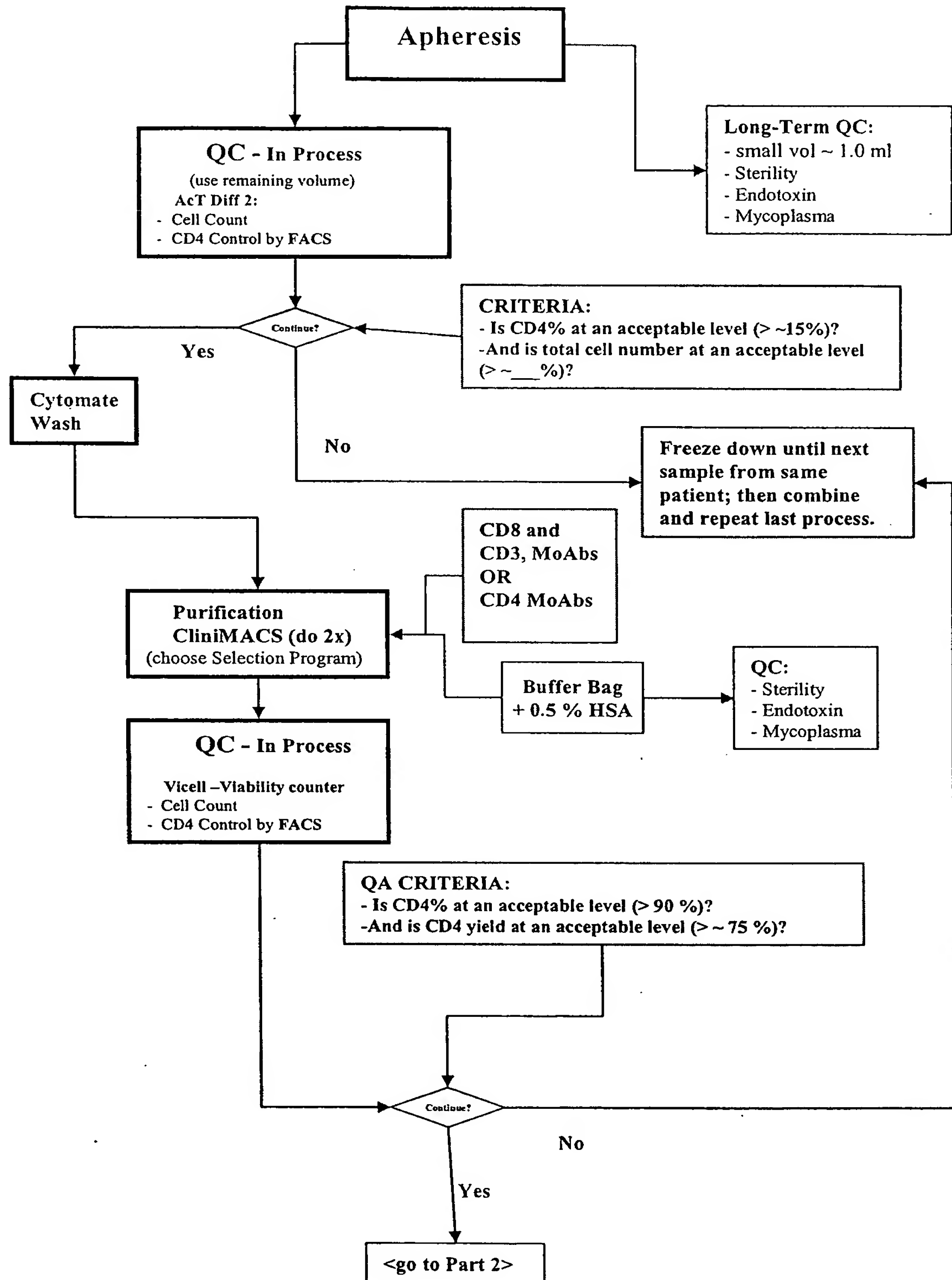


Figure 16A

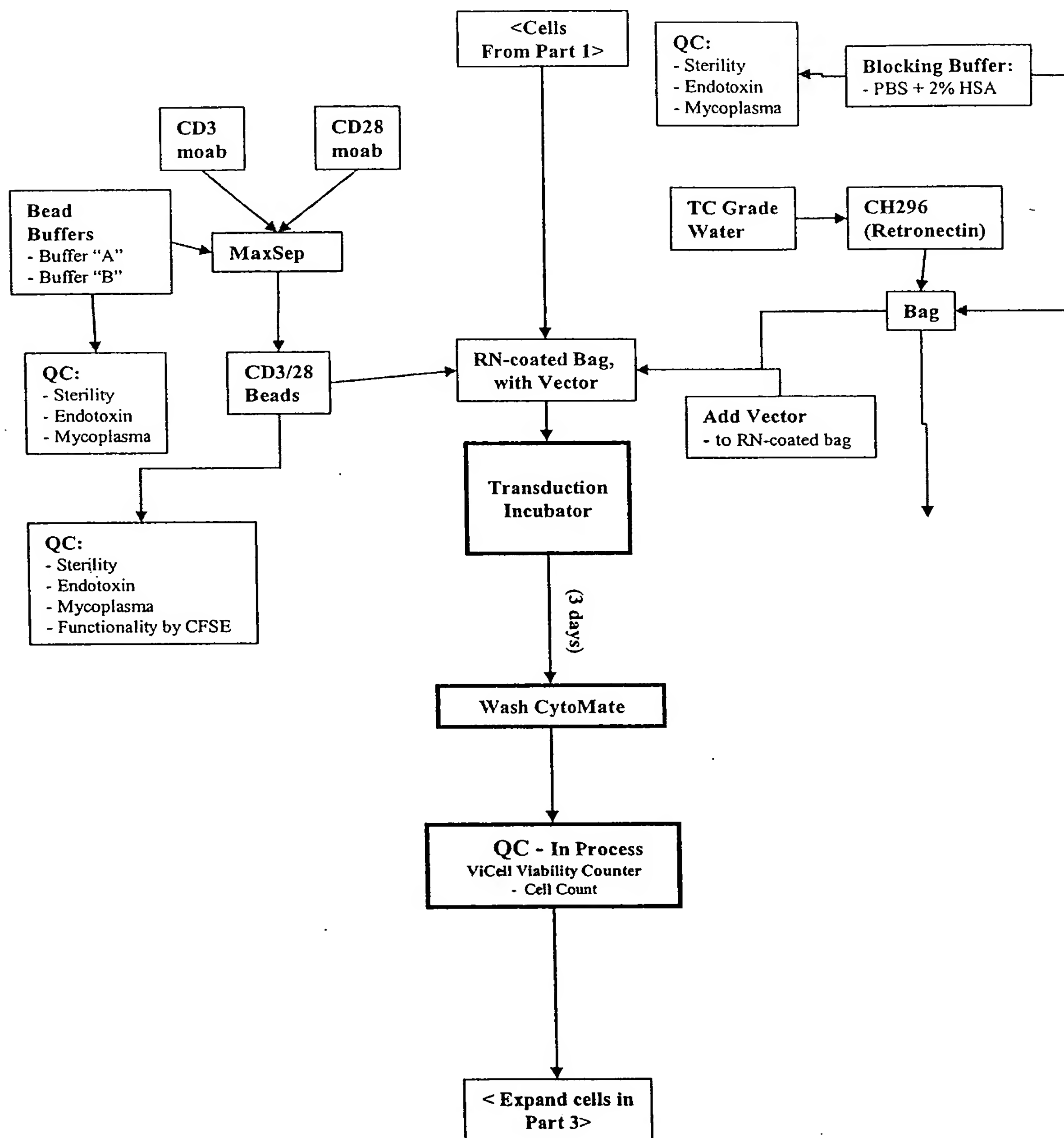


Figure 16B

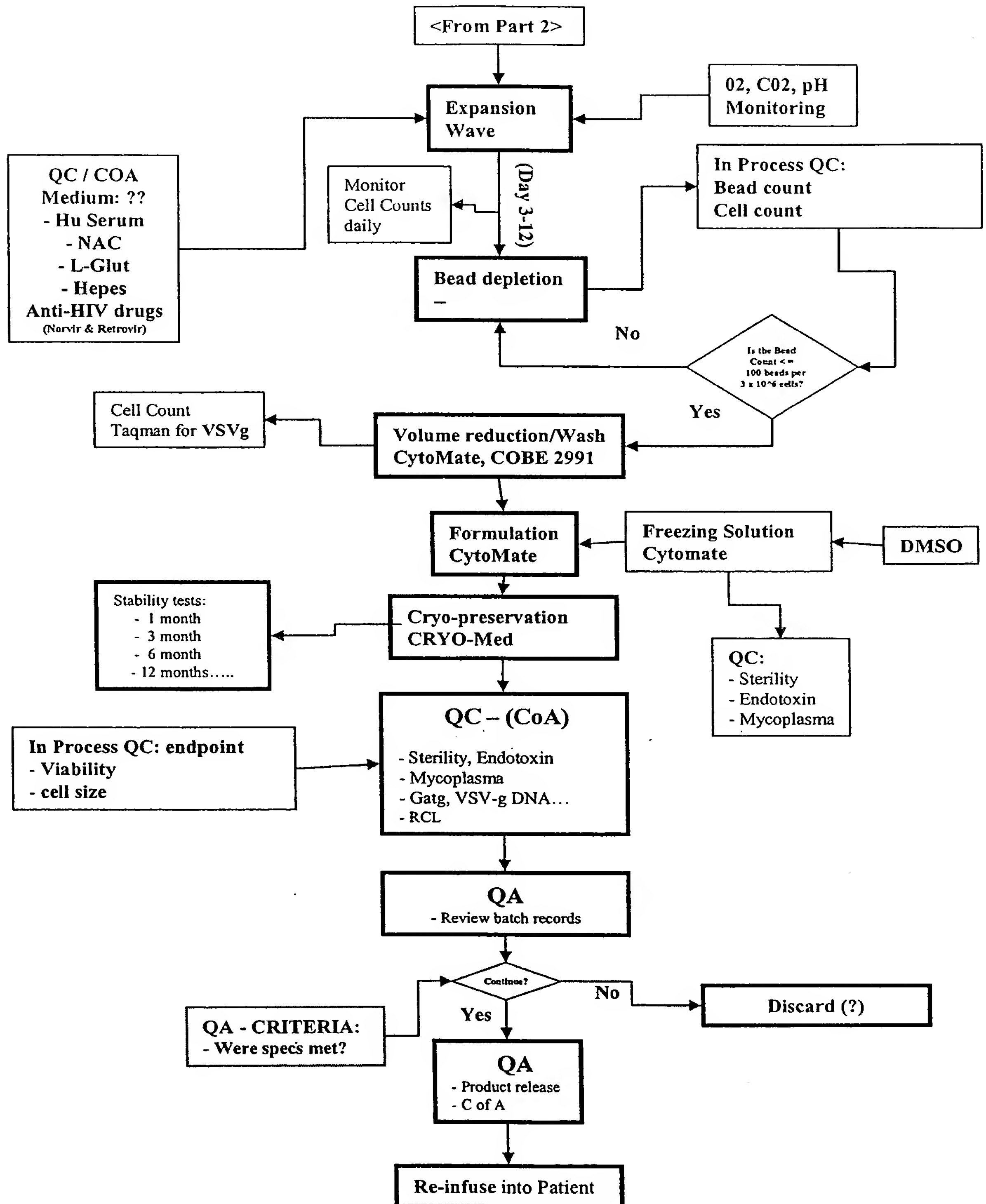


Figure 16C

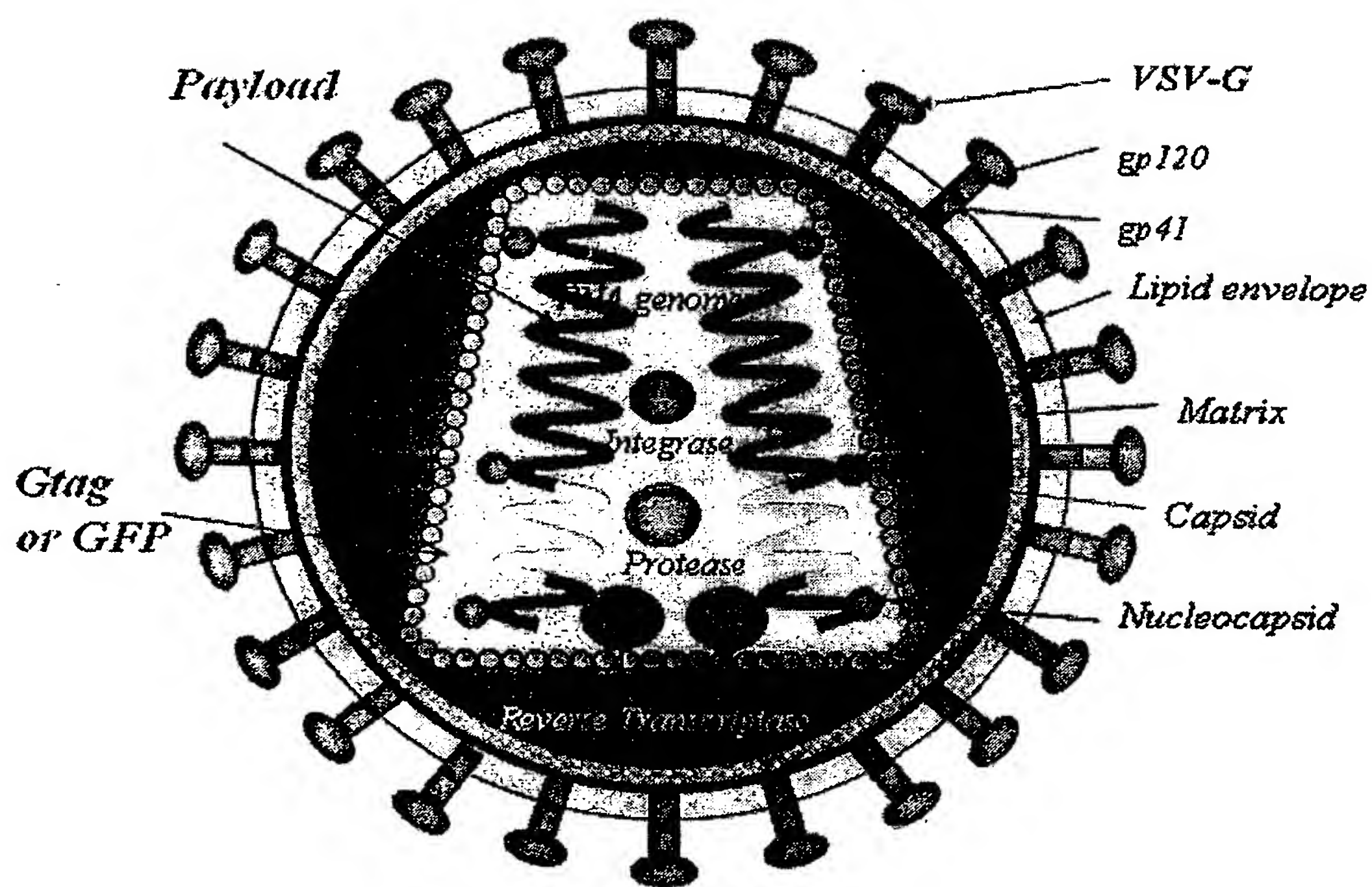


Figure 17

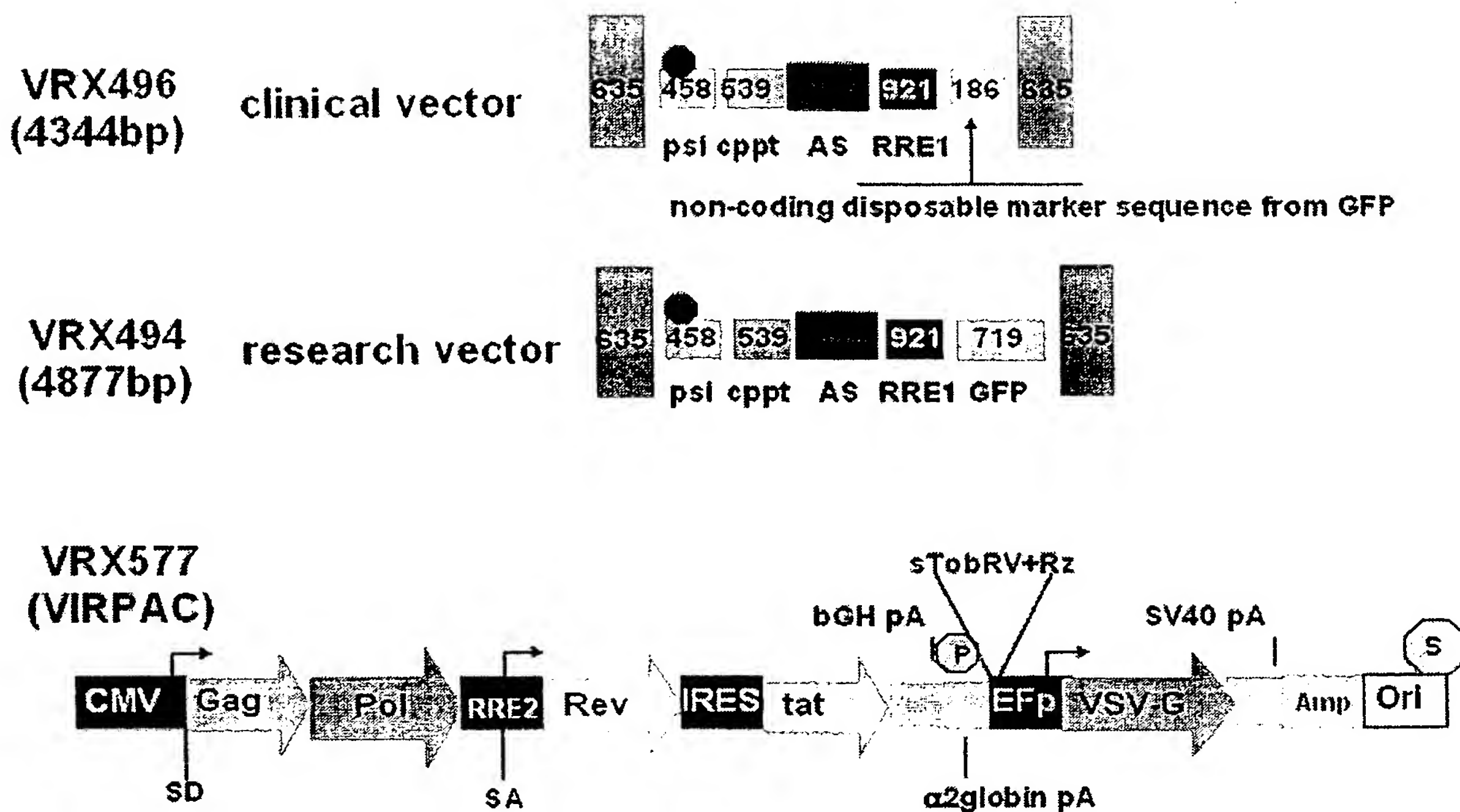


Figure 18

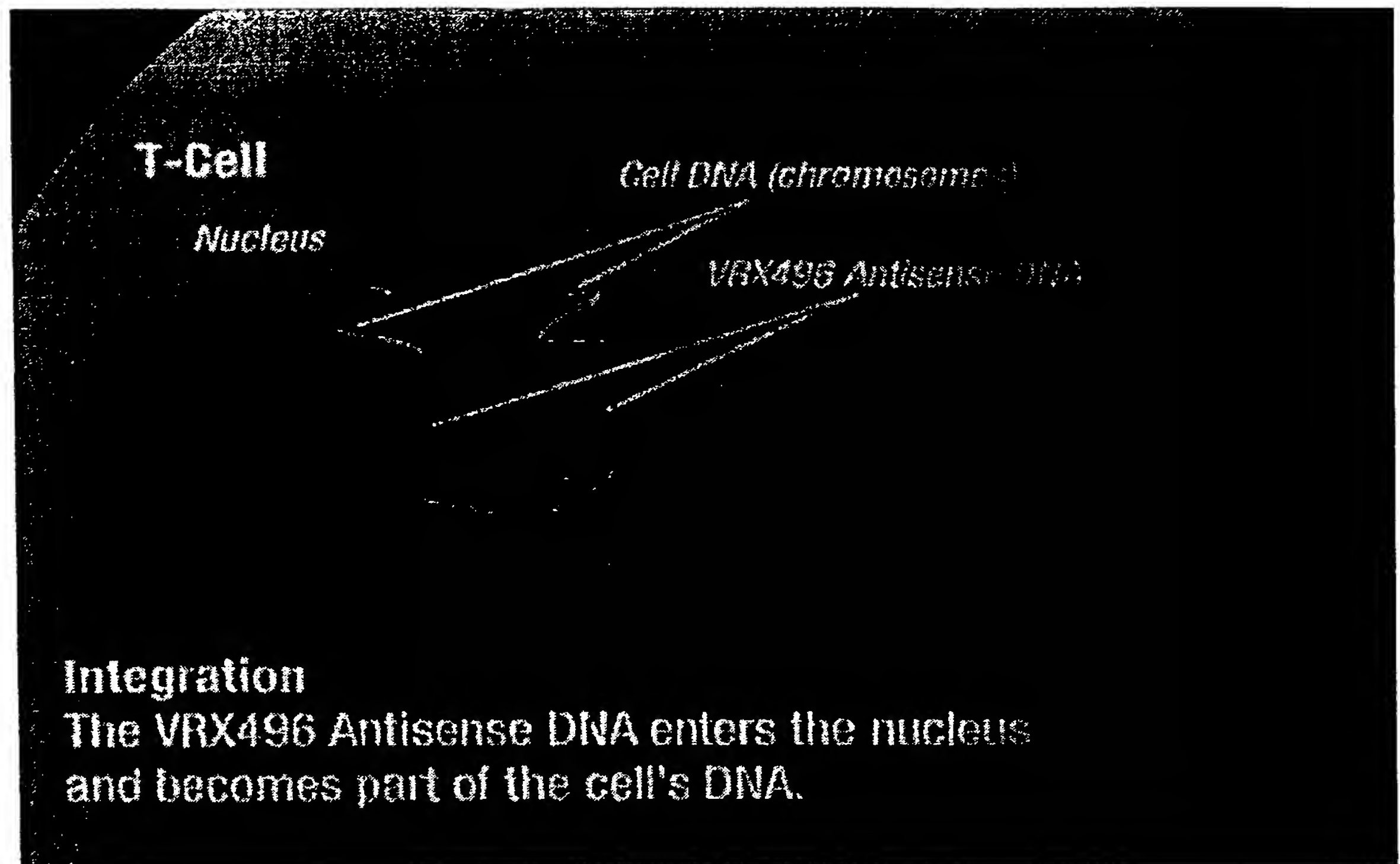


Figure 19

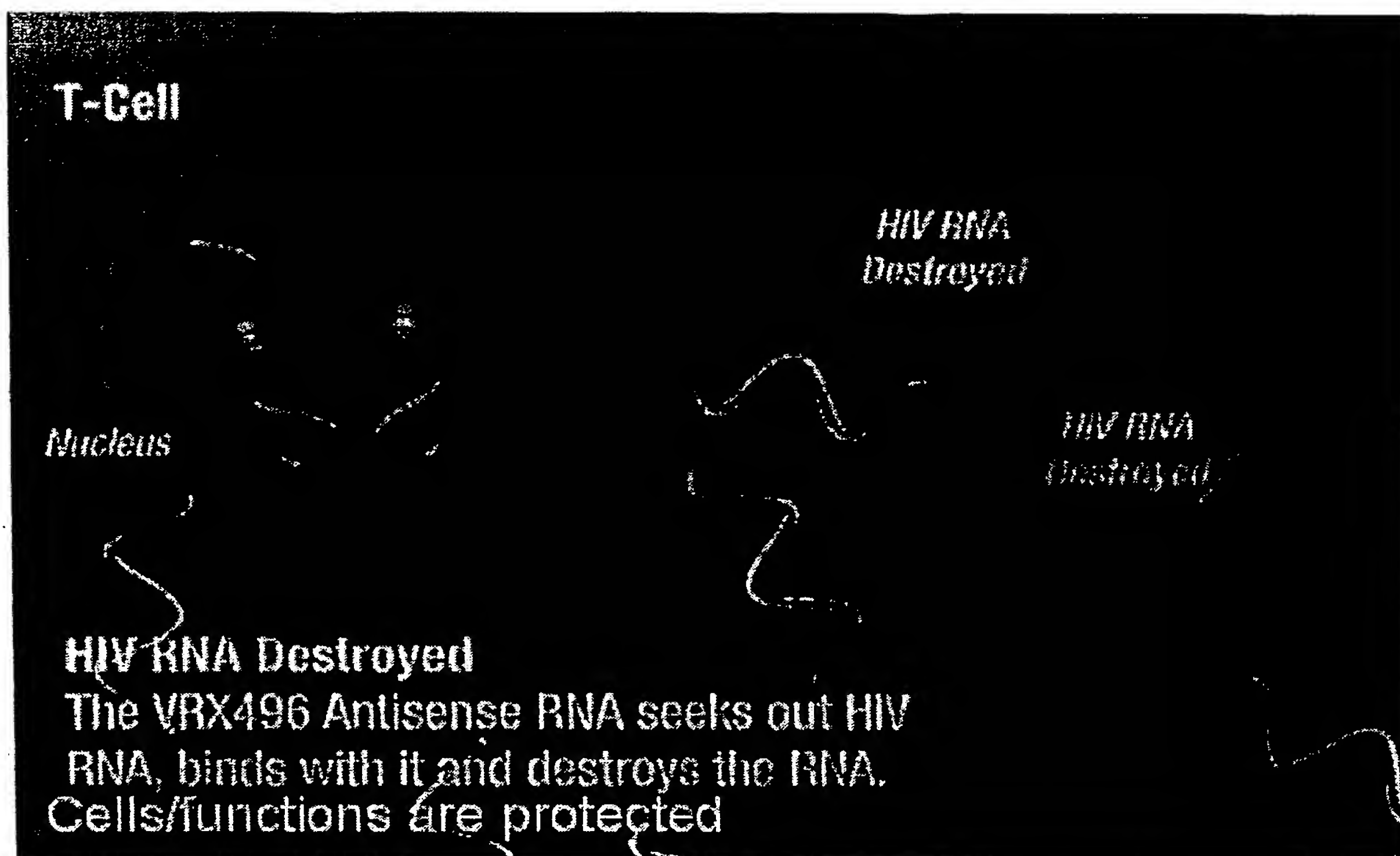


Figure 20

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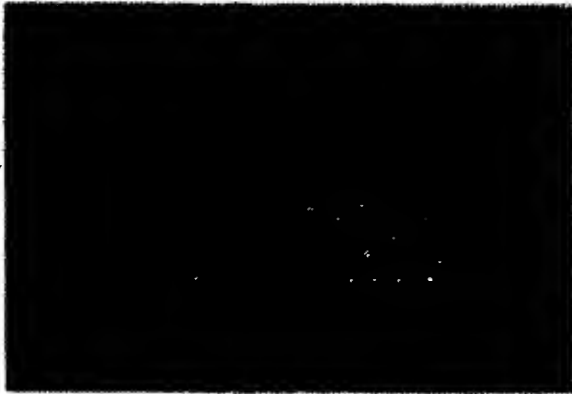

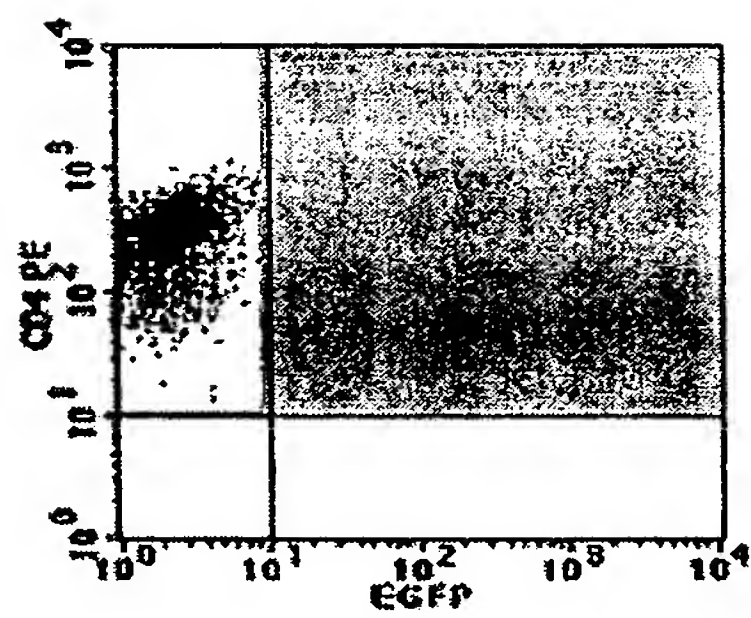
<ul style="list-style-type: none">◦ Anti HIV drugs<ul style="list-style-type: none">– 2-8 binding sites		Number of Mutations Needed for Resistance	Ability to Cause Disease
		Small	High
<ul style="list-style-type: none">◦ Long antisense RNA<ul style="list-style-type: none">– 937 binding sites		Large	Low
HIV either gets destroyed by antisense or it mutates to levels where the virus is not fit to cause disease			

Figure 21

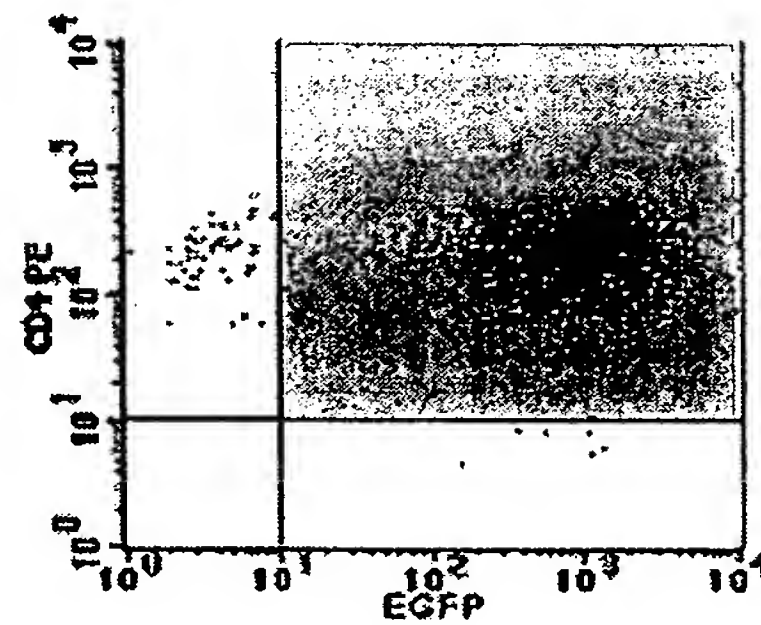


**Fluorescent Microscopic
View of GFP-expressing
vector (Humeau et al.
Mol Ther, 2004)**



0%

Control



>99%

+ vector-EGFP

Figure 22

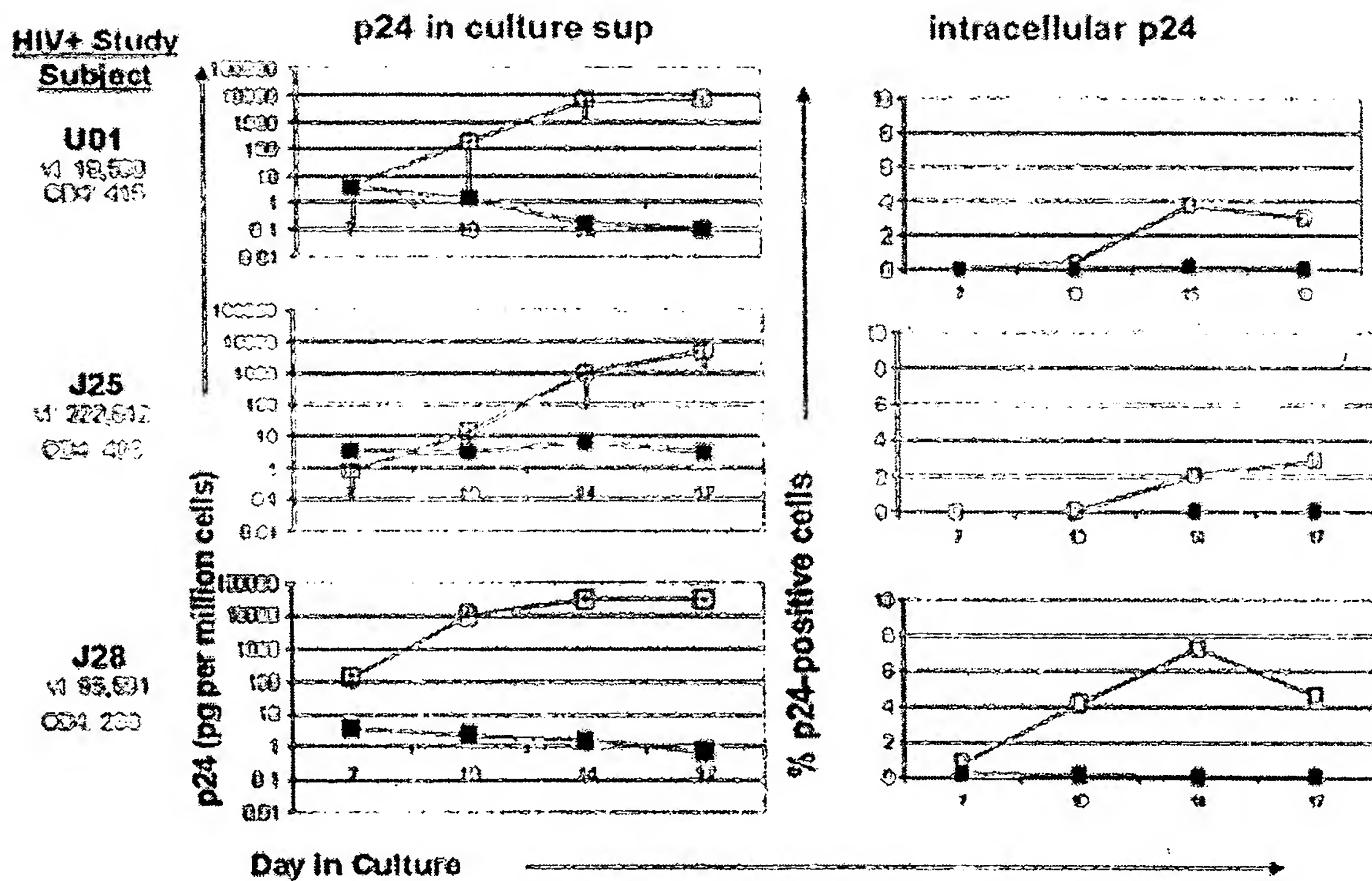


Figure 23

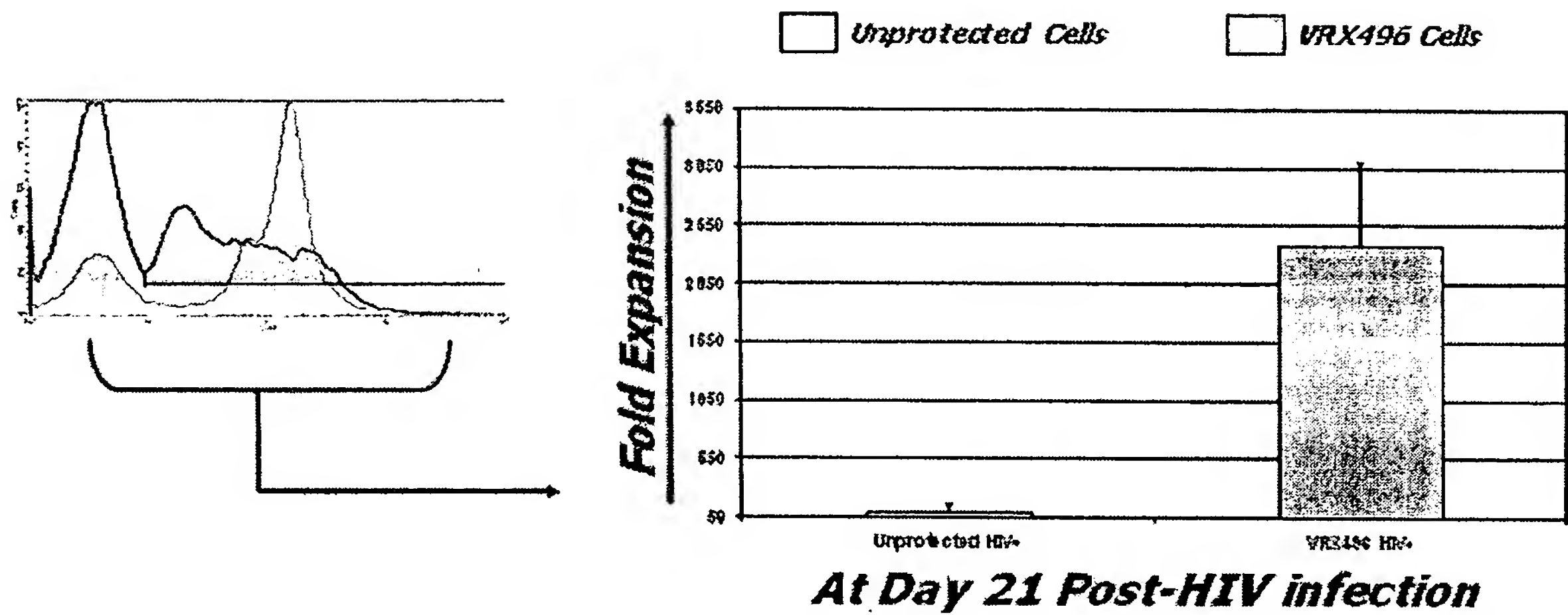


Figure 24

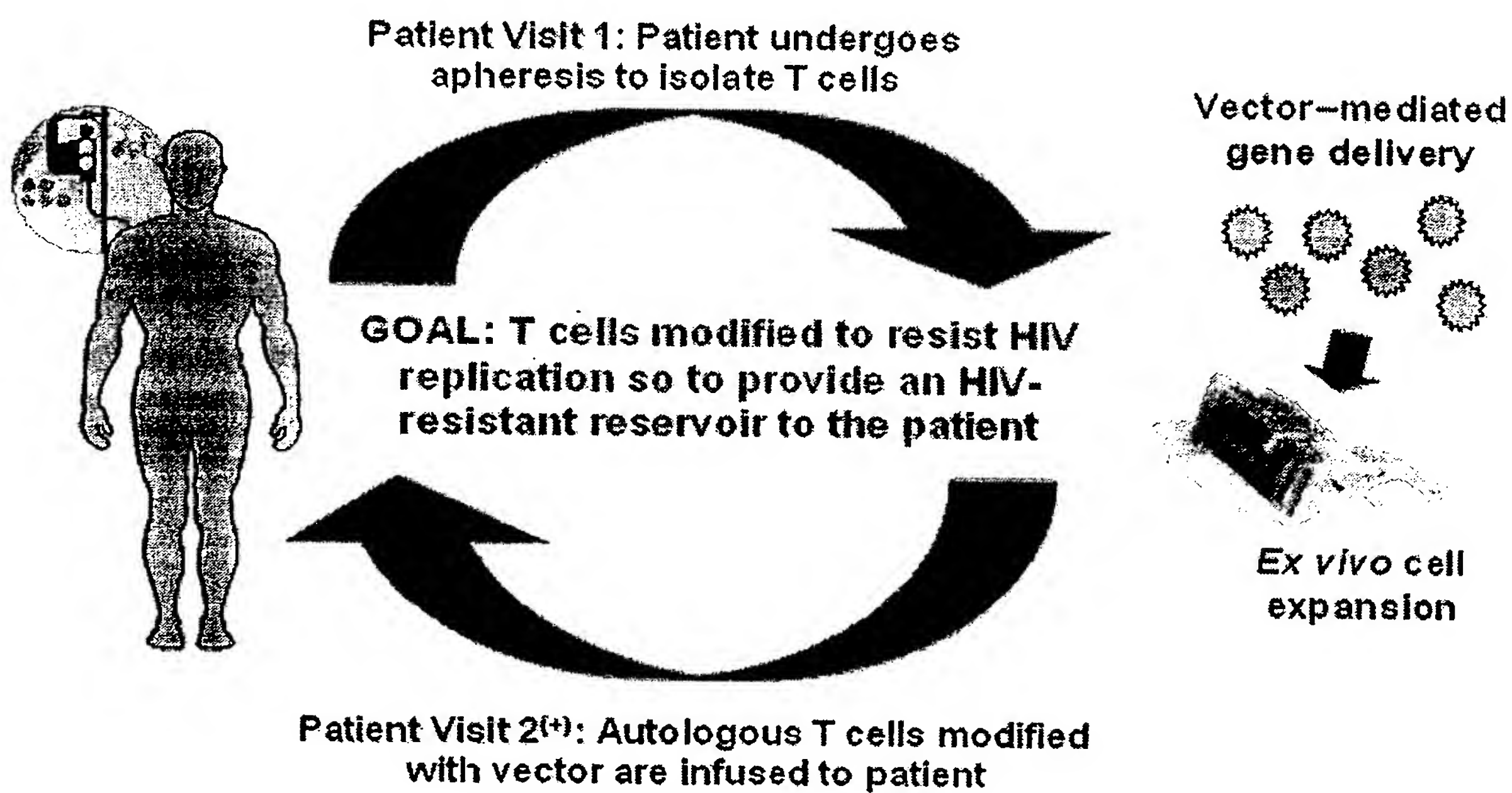


Figure 25

Table 1. Baseline characteristics of HIV subjects

Characteristics	#1 RB	#2 JFJ	#3 RAG	#4 AJ	#5 JF
Age	41	44	40	27	45
Gender	M	M	M	M	M
Ethnic Group	Caucasian	Caucasian	African American	African American	Caucasian
Mean viral load	188,500	64,100	46,150	54,213	19,972
Mean CD4 counts	228	316	241	308	220
HIV Infection (Yrs)	15	15	15	10	9
Discontinued Therapy	6 NRTI + 2 NNRTI + 5 PI	5 NRTI + 4 PI	6 NRTI + 1 PI	4 NRTI + 2 NNRTI + 1 PI	4 NRTI + 1 NNRTI + 1 PI
Current Therapy	2 NRTI + 2 PI	3 NRTI + 1 NNRTI + 1 PI	None	2 NRTI + 1 NRTI	2 NRTI + 1 PI

Figure 26

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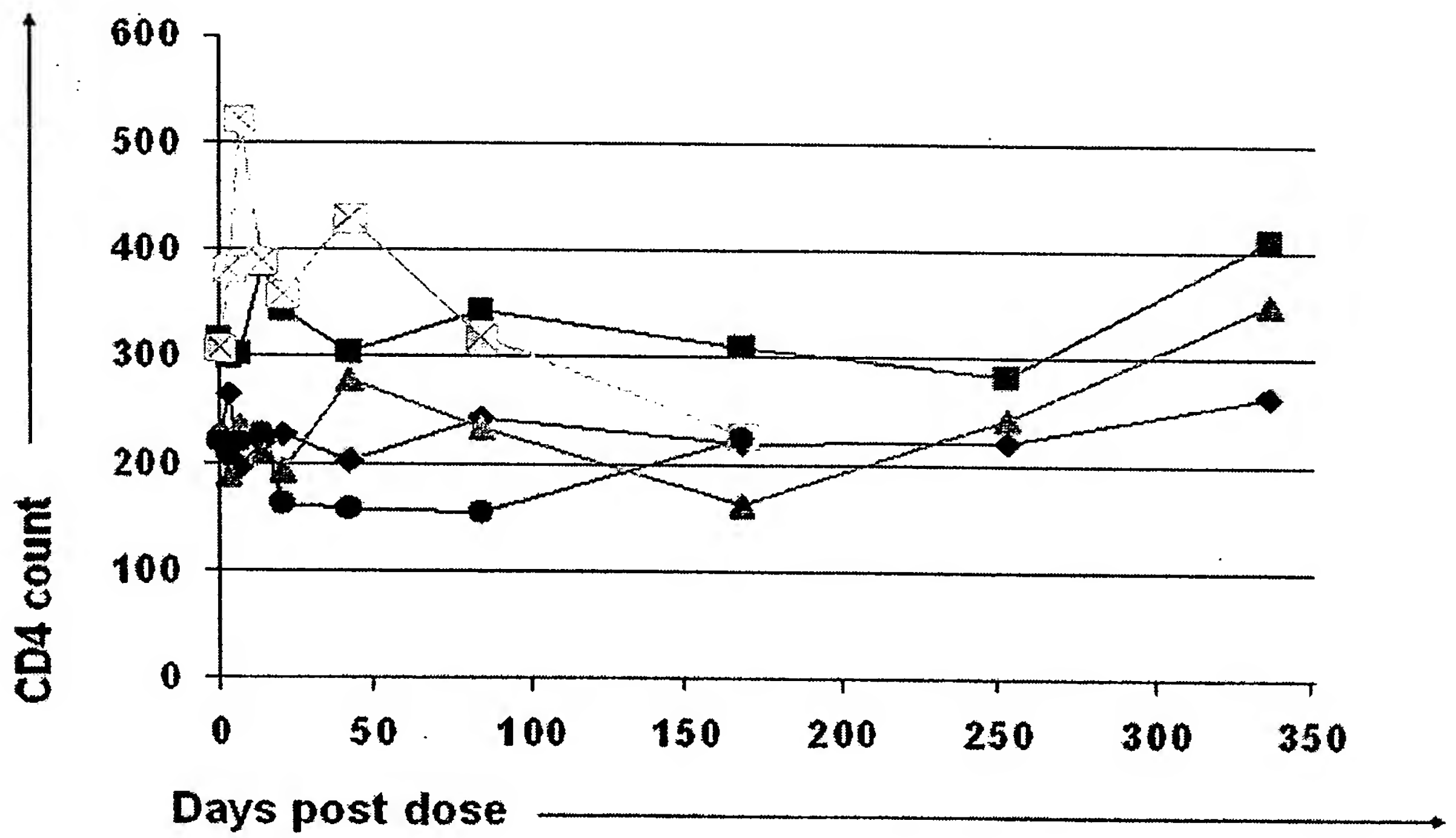


Figure 27

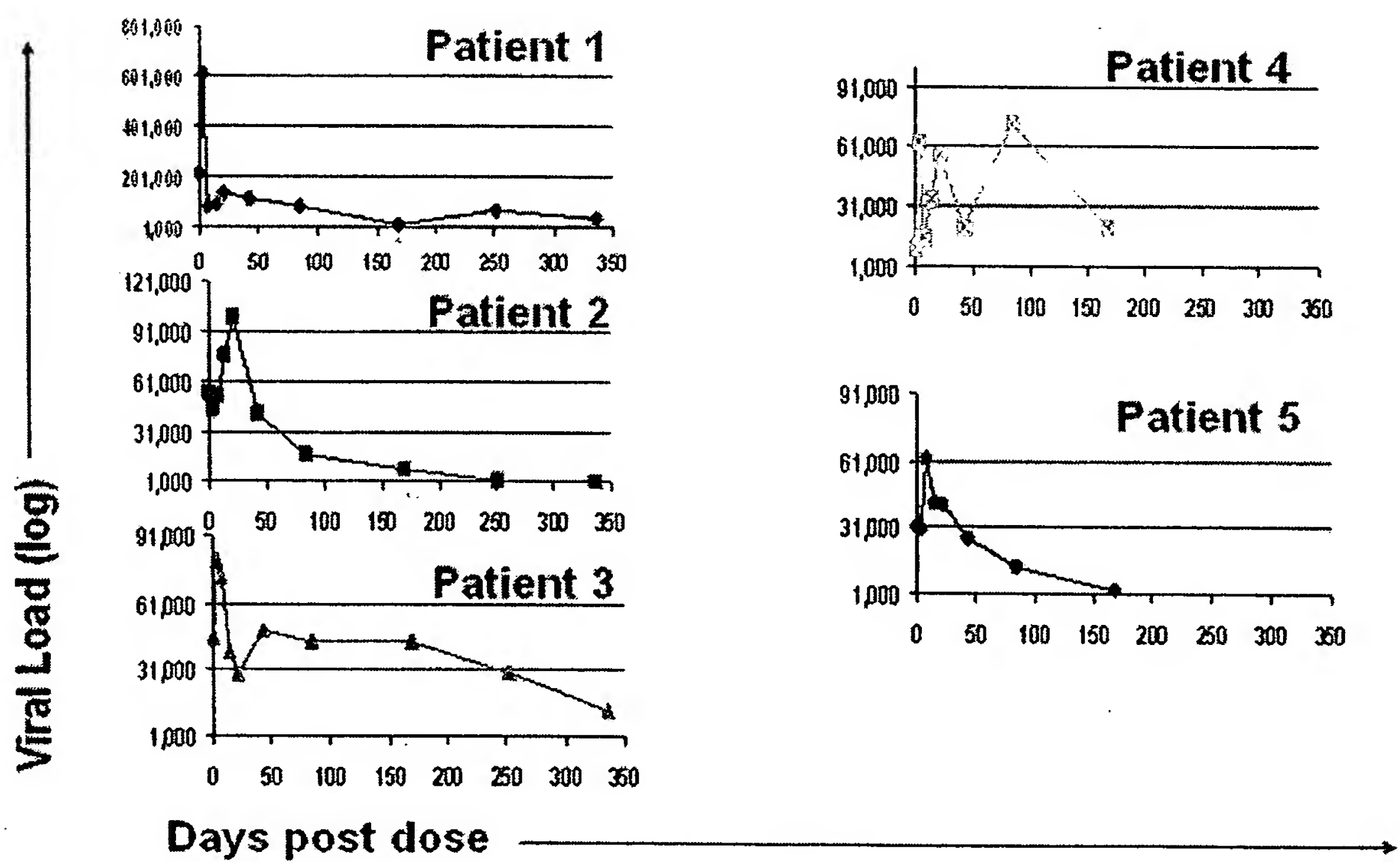


Figure 28

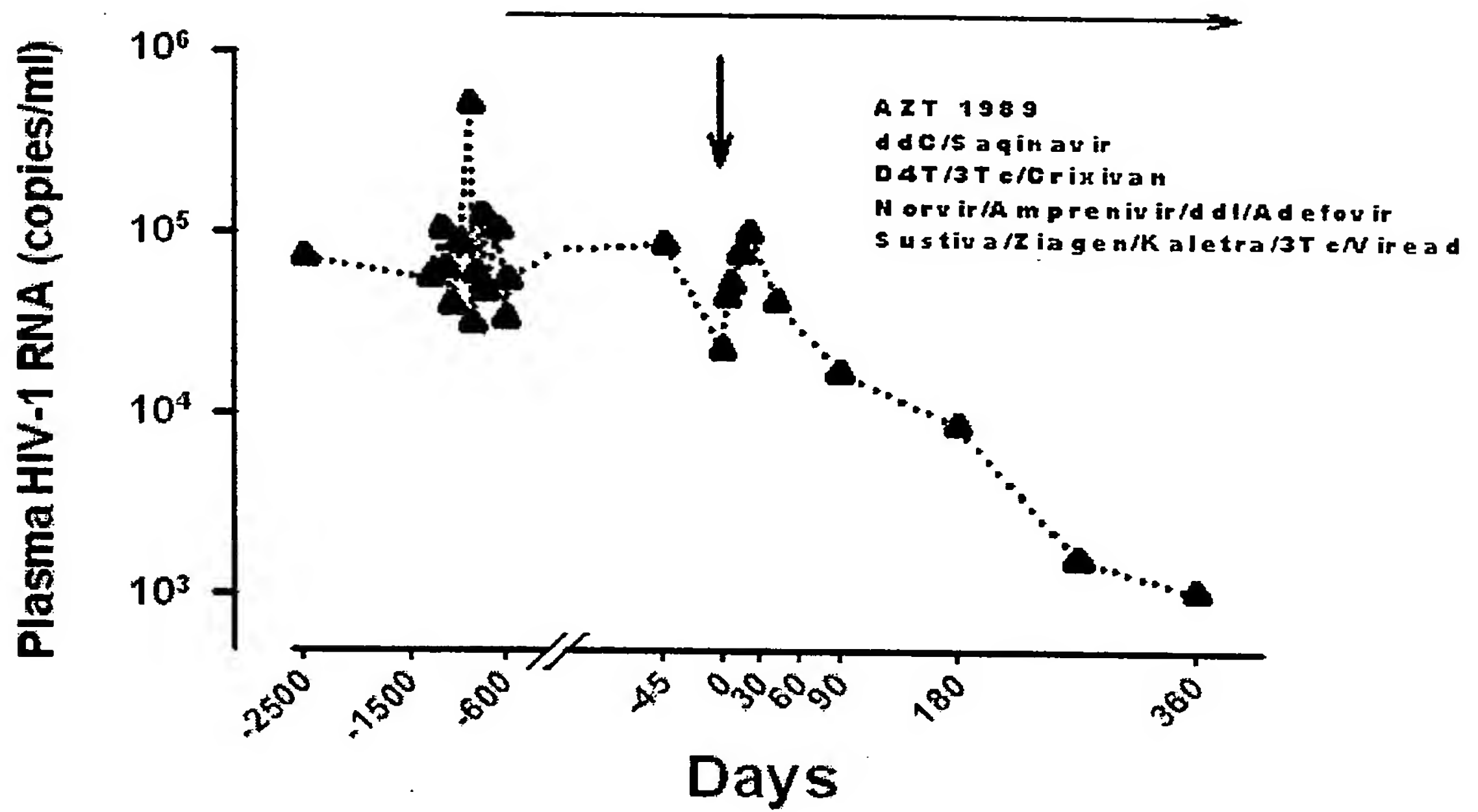


Figure 29

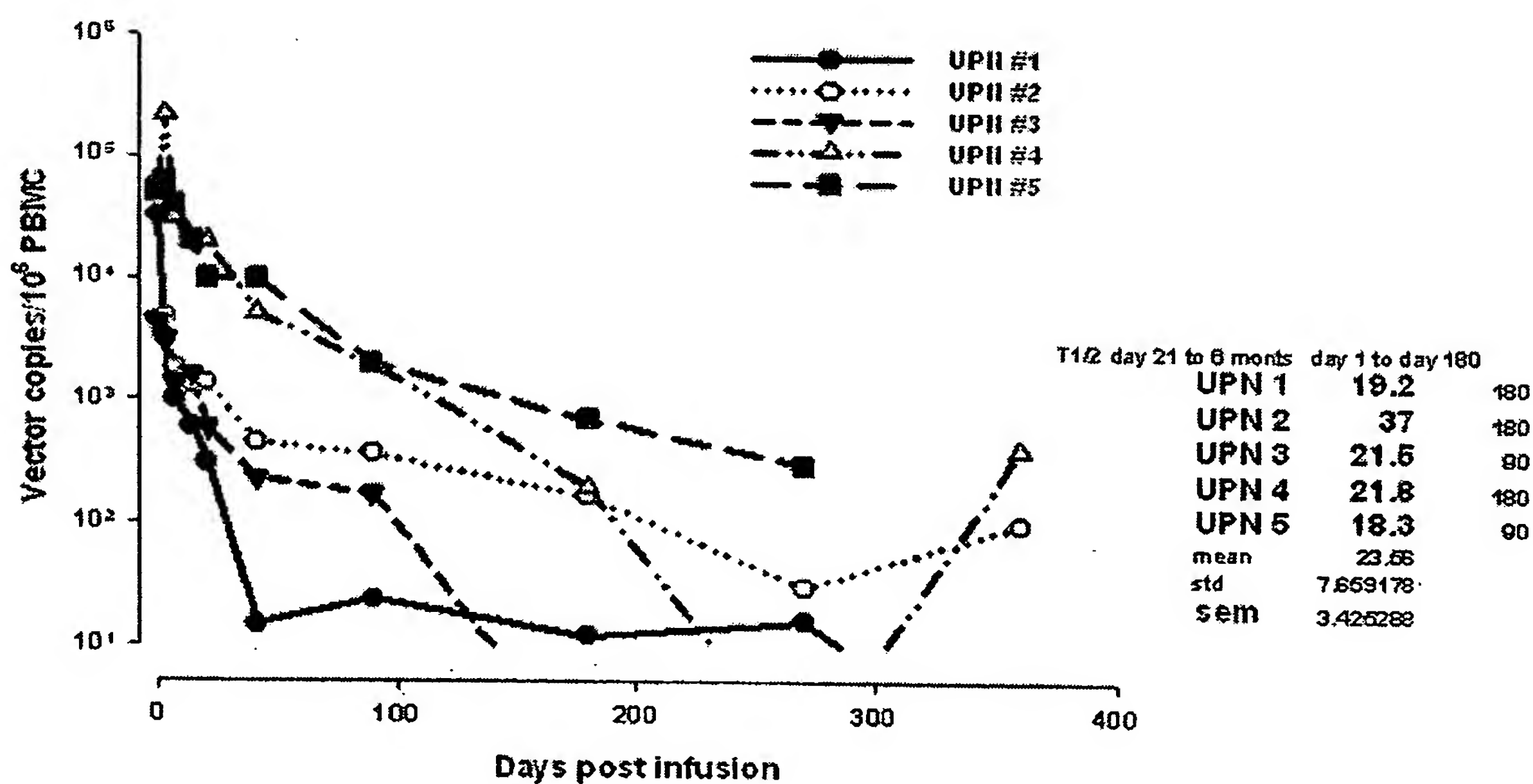


Figure 30

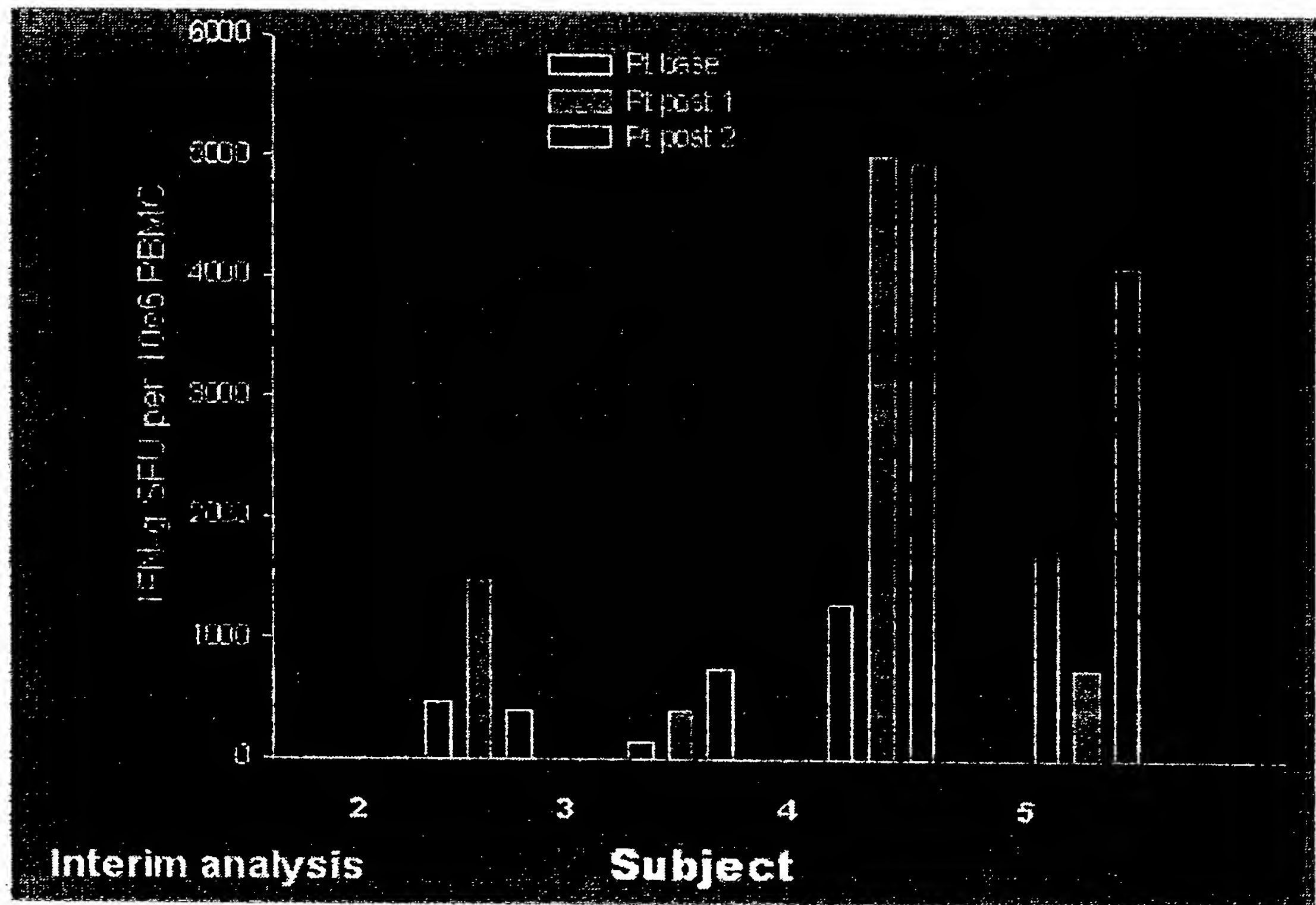


Figure 31

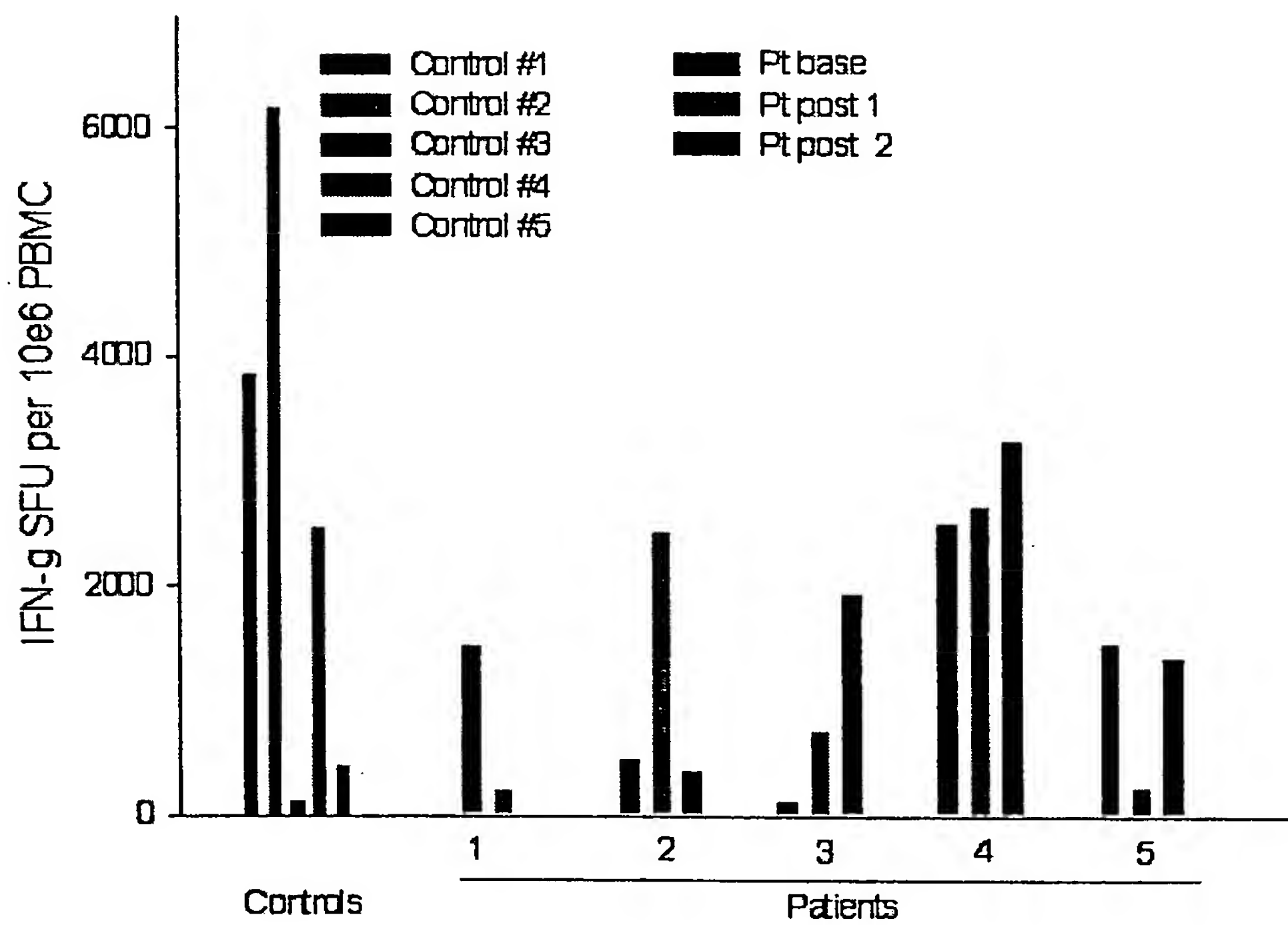


Figure 32

Parameter	Phase I Production	Phase II Production
Media	with 10% FBS	with 5% FBS
Transfection	individual cell factory per bag	8 cell factories per bag
Nunc Cell Factories	16	32
Harvest Collections	2	3
Harvest Volume	~35 L	~ 105L
Collections Mode	Individual NCF	8 NCF per bag
Clarification Filters	2 ft ²	5 ft ²
Concentration	~40 fold	~ 100 fold
Chromatography	4 separate 1L columns	2 serially connected 5L columns
Final volume	~1.2 L	~ 2.5 L

Figure 33

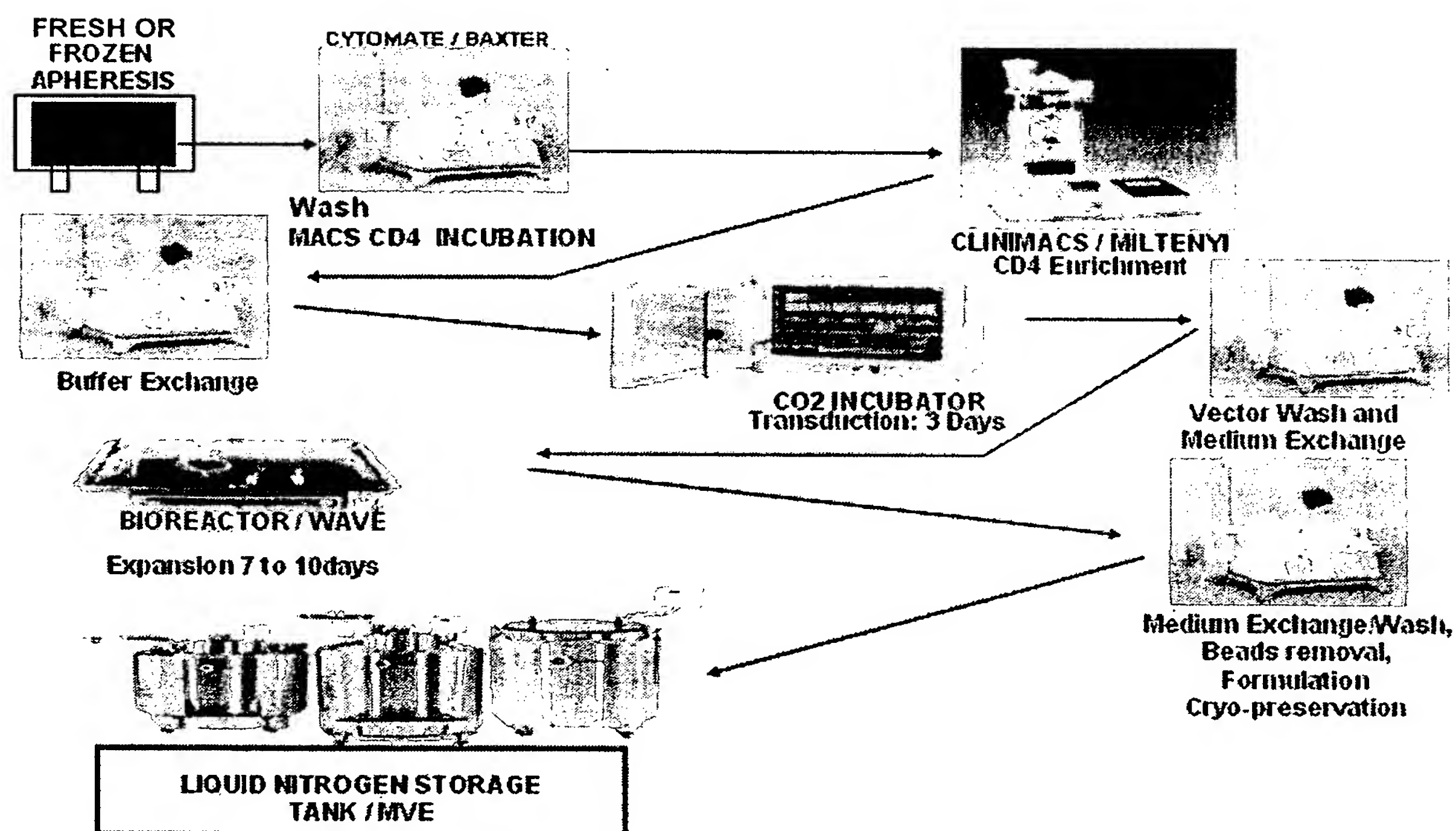


Figure 34

UPenn Phase 1 Cell Product	VIRxSYS Phase 2 Development Lots
CD4+ Cells: 56%, Abs. 3.06×10^8 (52 % recovery)	CD4+ purity: 97.62%, Abs. 3.42×10^9 (47.7% recovery)
CD4+ Cells: 52.2%, Abs. 4.38×10^8 (48% recovery)	CD4+ purity: 97.4%, Abs. 1.48×10^9 (40.5% recovery)
CD4+ Cells: 23%, Abs. 1.67×10^8 (26% recovery)	CD4+ purity: 91.77%, Abs. 2.05×10^9 (48.8% recovery)
CD4+ Cells: 33.4%, Abs. 2.93×10^8 (30% recovery)	
CD4+ Cells: 19.5 %, Abs. 1.77×10^8 (23% recovery)	
Average CD4+purity: 36.82% (range 19.5-56%)	Average CD4+ purity: 95.6% (recovery 91.77-97.62%)

Figure 35

Phase I Cell Product		Phase II Development Lots	
Subject Study ID	Vector copy number per cell	Process Run #	Vector copy number per cell
001-022 J-K	1.20	1	2.80
001-017 A-J	4.10	2	1.19
001-010 RAG	0.98	3	1.48
001-001 JFJ	1.80		
001-002 R-B	2.3		
Average	2.08		1.82

Figure 36

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Phase I Cell Product		Phase II Development Lots	
Subject Study ID	Total Cells / Fold Expansion	Process Run #	Total Cells / Fold Expansion
001-022 J-K	15.8x10 ⁹ / 65	1	52.3x10 ⁹ / 28.6
001-017 A-J	20.6x10 ⁹ / 40	2	104x10 ⁹ / 58.8
001-010 RAG	6.8x10 ⁹ / 25	3	96.6x10 ⁹ / 63
001-001 JFJ	11.5x10 ⁹ / 32	4	87.5x10 ⁹ / 63.2
001-002 R-B	15.2x10 ⁹ / 66		
Average	14x10 ⁹ / 45.6		85.1x10 ⁹ / 53.4

Figure 37

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